US005743863A

United States Patent [19]

Chapelon

[11] Patent Number: 5,743,863

[45] Date of Patent: *Apr. 28, 1998

[54] **HIGH-INTENSITY ULTRASOUND THERAPY METHOD AND APPARATUS WITH CONTROLLED CAVITATION EFFECT AND REDUCED SIDE LOBES**

[75] Inventor: **Jean-Yves Chapelon**, Villeurbanne, France

[73] Assignee: **Technomed Medical Systems and Institut National**, Vaux en Velin

[*] Notice: The term of this patent shall not extend beyond the expiration date of Pat. No. 5,573,497.

[21] Appl. No.: **720,555**

[22] Filed: **Oct. 2, 1996**

Related U.S. Application Data

[63] Continuation of Ser. No. 396,160, Feb. 28, 1995, Pat. No. 5,573,497, which is a continuation-in-part of Ser. No. 307,719, Nov. 30, 1994, abandoned.

[30] **Foreign Application Priority Data**

Jan. 22, 1993	[FR]	France	9300662
Jan. 3, 1994	[FR]	France	9402322
Jan. 21, 1994	[WO]	WIPO	PCT/FR94/00070

[51] **Int. Cl.**[6] **A61B 17/00**

[52] **U.S. Cl.** **601/2**; 601/3

[58] **Field of Search** 128/660.03; 601/2, 601/3; 607/97

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,866,068	2/1975	Krenicki et al. .	
5,501,655	3/1996	Rolt et al.	601/2 X
5,573,497	11/1996	Chapelon	601/2

FOREIGN PATENT DOCUMENTS

0274136	12/1987	European Pat. Off. .
2685211	12/1991	France .
2524555	5/1975	Germany .

OTHER PUBLICATIONS

"Effects of cavitation in the high intensity therapeutic ultrasound", *Proceedings of 1991 Ultrasonics Symposium*, vol. 1, Dec. 1991, pp. 1357–1360.

"Cavitation threshold measurements for microsecond long pulses of ultrasound", *Journal of the Acoustical Society of America*, vol. 83, No. 6, Jun. 1988, pp. 2190–2201 Copy of international search report.

Primary Examiner—Francis Jaworski

Attorney, Agent, or Firm—Welsh & Katz, Ltd.

[57] **ABSTRACT**

In a high-energy ultrasound therapy method and apparatus, said apparatus comprises a therapy device with at least one ultrasound therapy transducer element and a signal generator supplying an electronic signal to said ultrasound transducer element, the signal generator supplying the transducer(s) with a wideband electronic signal of the random or pseudo-random type.

22 Claims, 5 Drawing Sheets

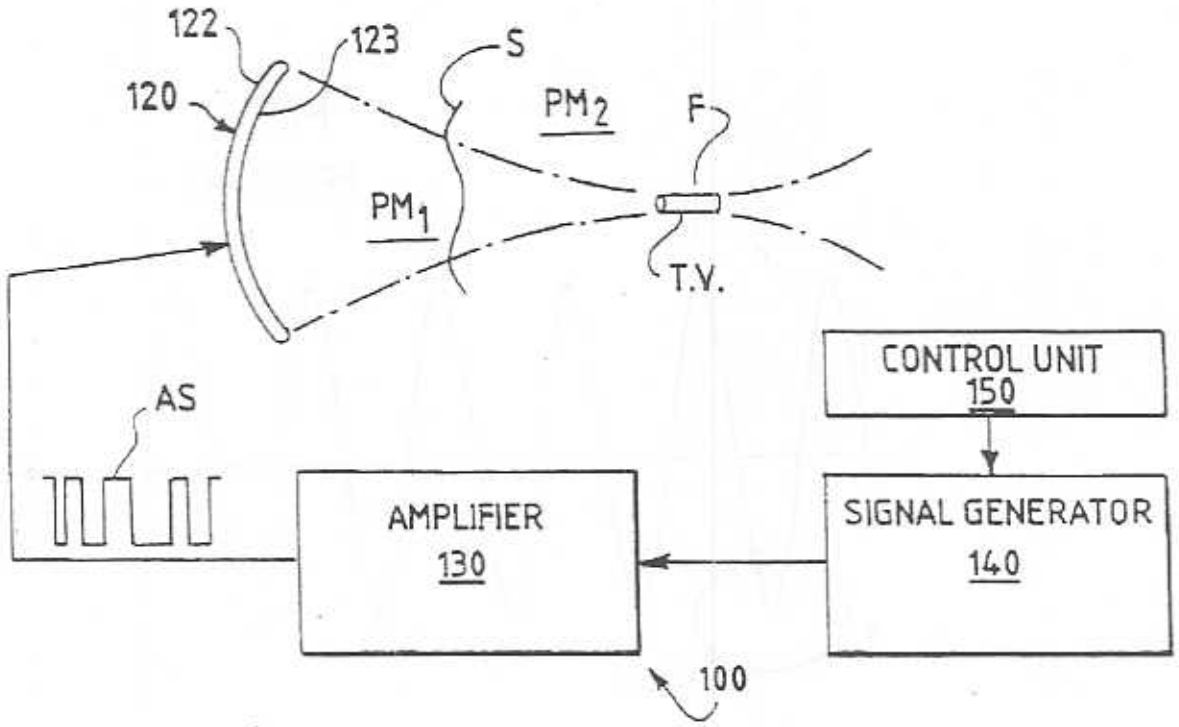


FIG. 1
PRIOR ART

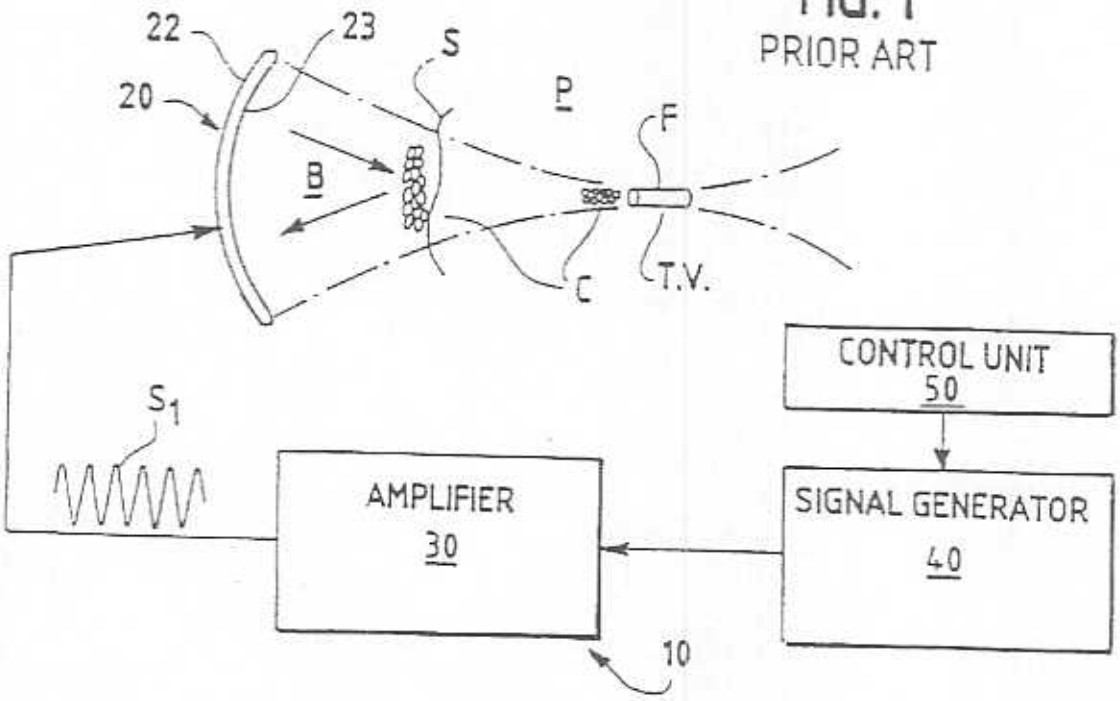


FIG. 2
PRIOR ART

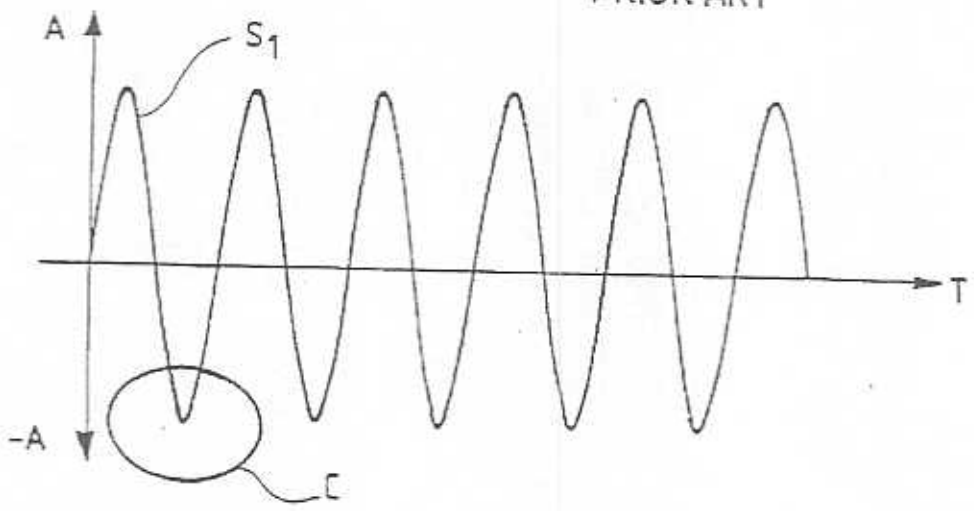


FIG. 1
PRIOR ART

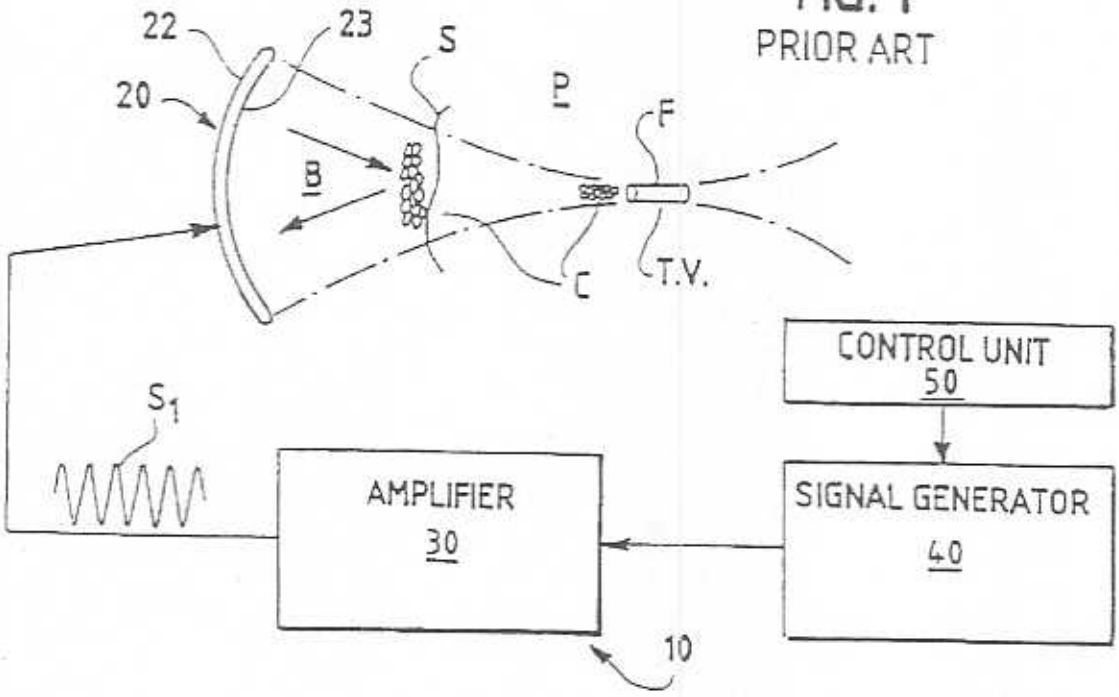


FIG. 2
PRIOR ART

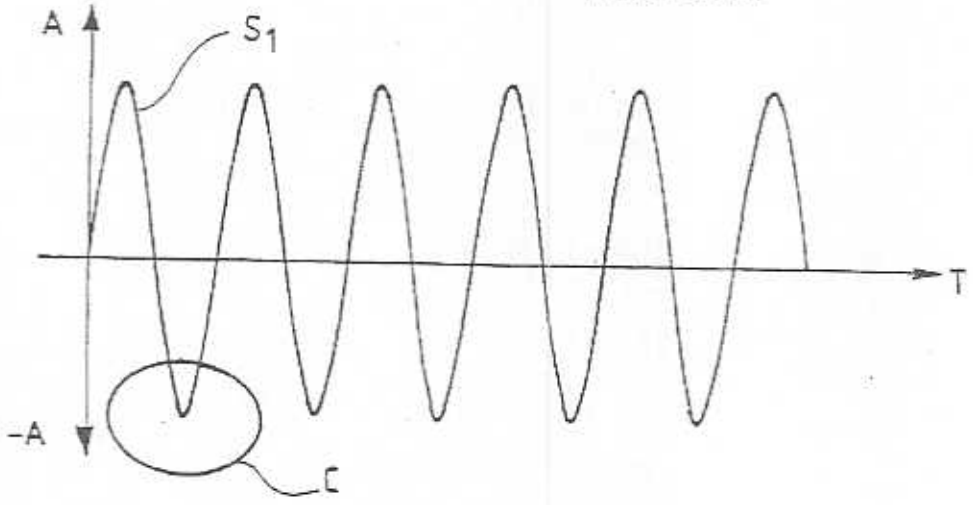


FIG. 3

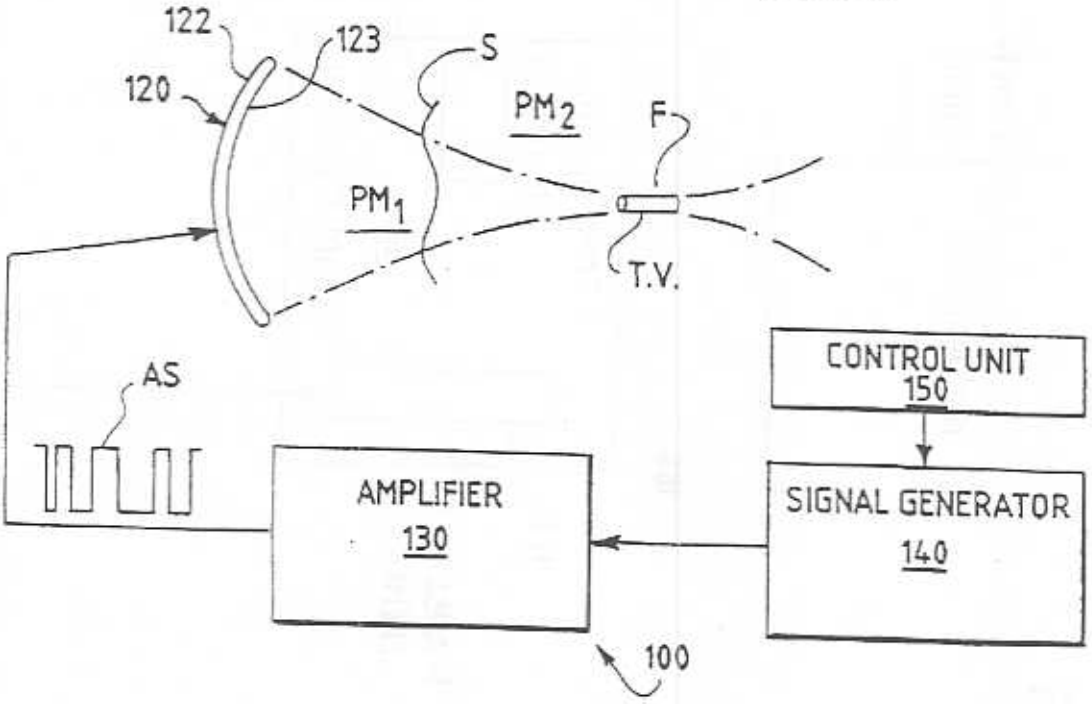

122
123
S
120
PM2
F
PM1
T.V.
AS
CONTROL UNIT
150
AMPLIFIER
130
SIGNAL GENERATOR
140
100

FIG. 4

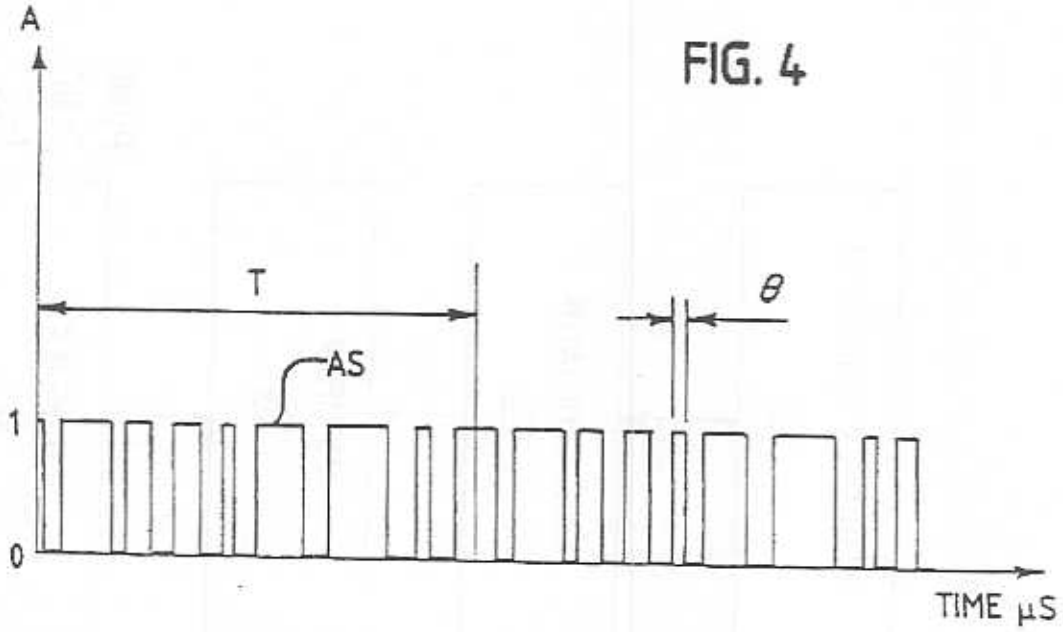

A
T
θ
AS
1
0
TIME μS

FIG. 5

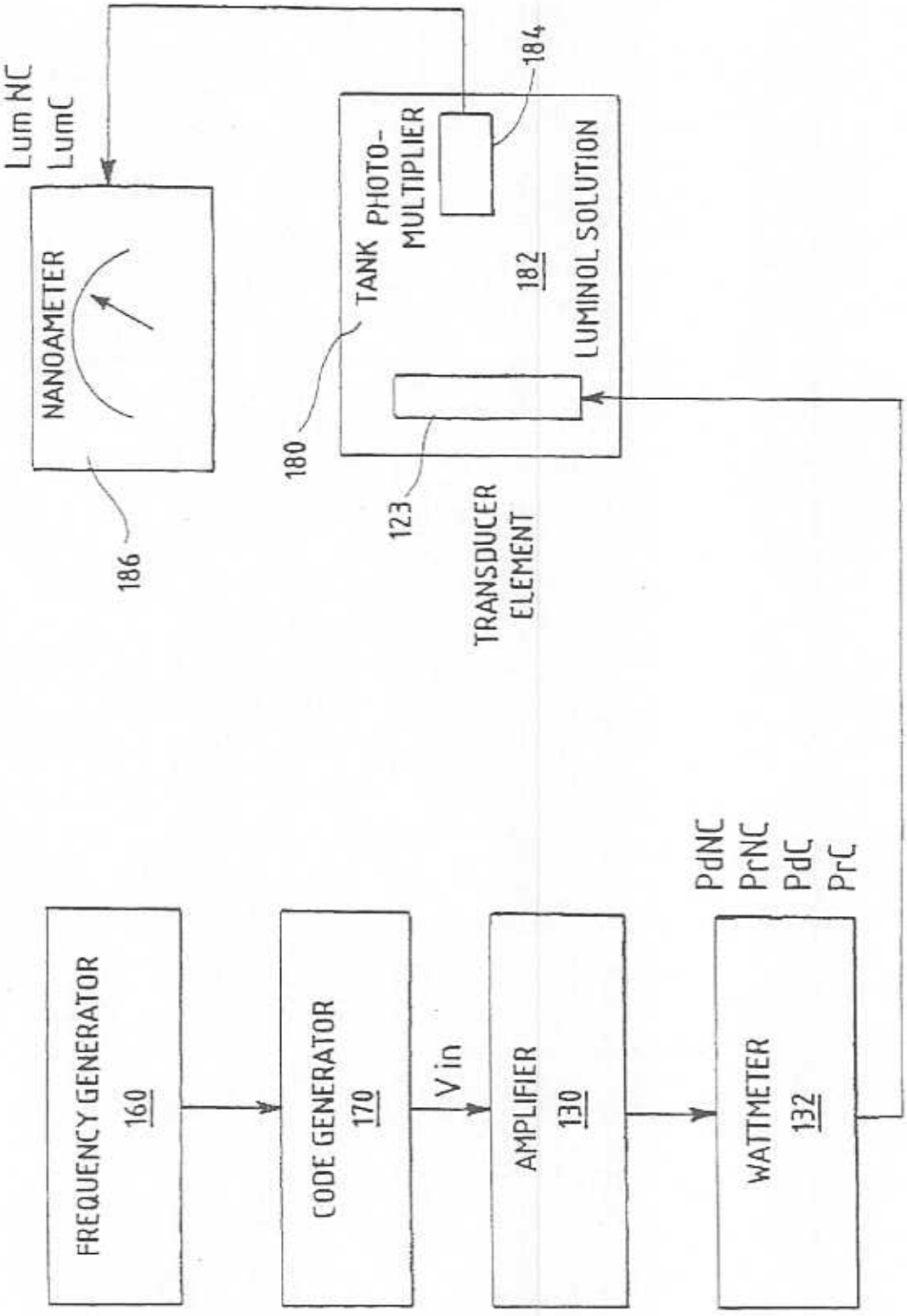

FREQUENCY GENERATOR
160
CODE GENERATOR
170
V in
AMPLIFIER
130
WATTMETER
132
PdNC
PrNC
PdC
PrC
TRANSDUCER ELEMENT
123
180
TANK
PHOTO-MULTIPLIER
184
182
LUMINOL SOLUTION
NANOAMETER
186
Lum NC
LumC

FIG. 6

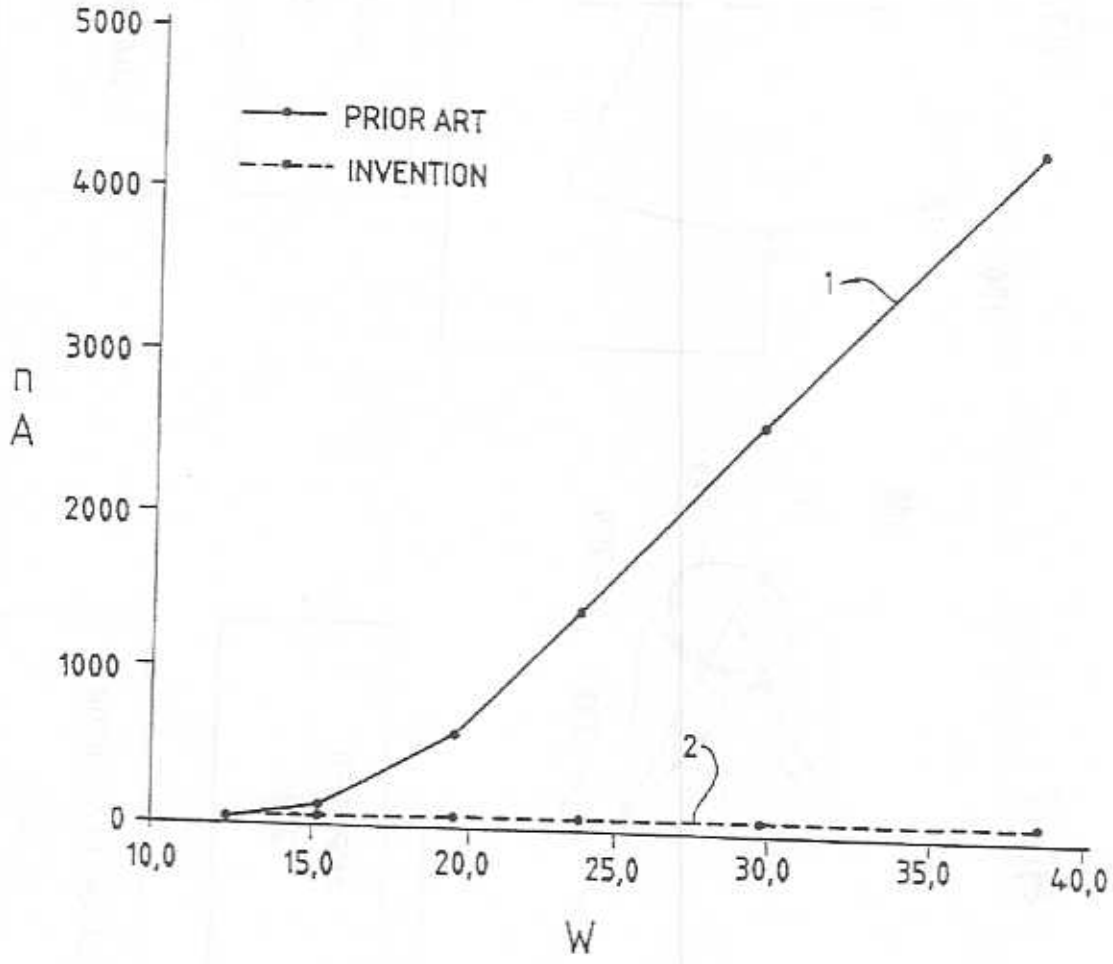

5000
4000
3000
2000
1000
0
PRIOR ART
INVENTION
1
2
n
A
10,0
15,0
20,0
25,0
30,0
35,0
40,0
W

FIG. 8

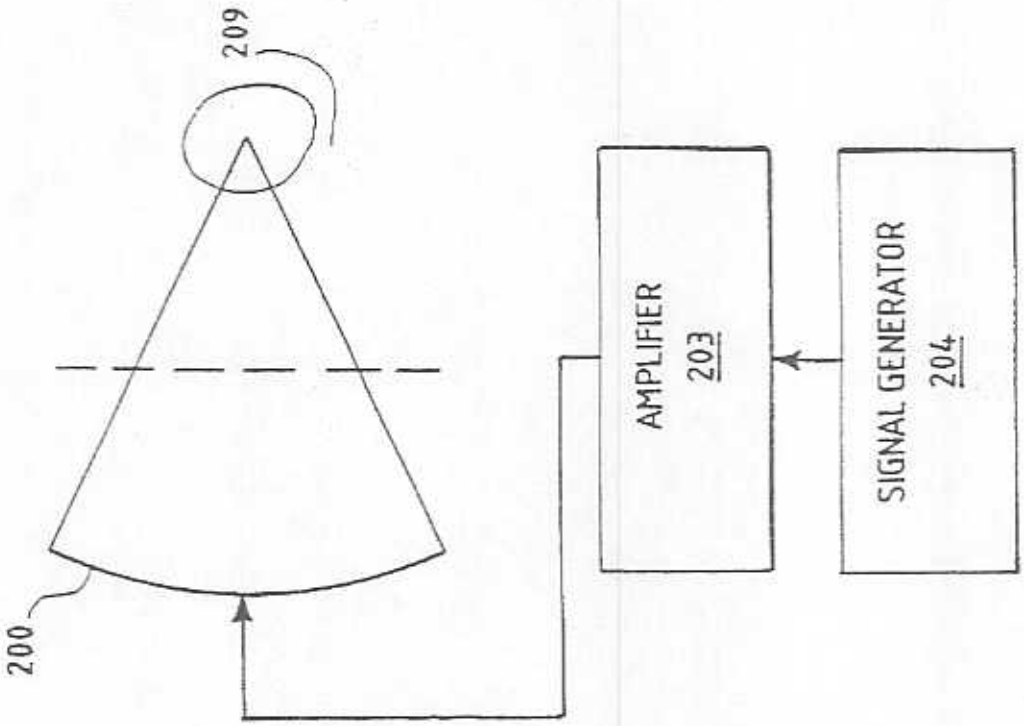
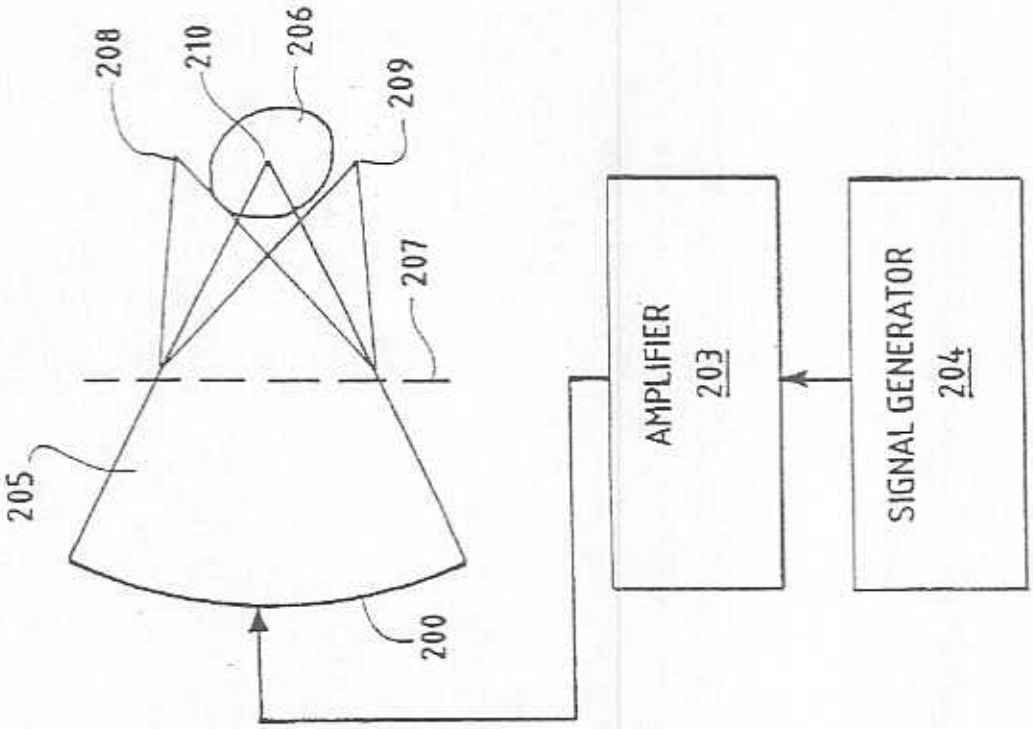

209
200
AMPLIFIER
203
SIGNAL GENERATOR
204

FIG. 7


208
210
206
209
207
205
200
AMPLIFIER
203
SIGNAL GENERATOR
204

HIGH-INTENSITY ULTRASOUND THERAPY METHOD AND APPARATUS WITH CONTROLLED CAVITATION EFFECT AND REDUCED SIDE LOBES

This patent application is a continuation of U.S. Ser. No. 08/396,160, entitled High Intensity Ultrasound Method and Apparatus with Controlled Cavitation Effect and Reduced Side Lobes, filed on Feb. 28, 1995 and issued as U.S. Pat. No. 5,573,497. U.S. Ser. No. 08/396,160 claims priority based on French Patent Application No. 94/02322 dated Mar. 1, 1994 and is a continuation-in-part of U.S. Ser. No. 08/307,719 and filed on Nov. 30, 1994 and now abandoned, which is based on PCT/FR94/00070 dated Jan. 21, 1994 which claims priority based on French Patent Application No. 93/00662 dated Jan. 22, 1993. The subject application claims priority based on all of the above United States and foreign applications.

BACKGROUND OF THE INVENTION

The present invention relates to a therapy method and apparatus for generating high-intensity ultrasound with control of cavitation effect, and to the use of this method and apparatus for reducing secondary lobes set up by a periodic-type structure.

It is known that ultrasound therapy, using a piezoelectric transducer driven by sinewave-type electronic signals makes it possible to create tissue lesions through tissue heating due to ultrasound absorption. Furthermore, such tissue lesions can be limited to a specific volume by carrying out therapy using focused ultrasound, which is particularly valuable for achieving effective treatment in cancer therapy such as, for example, cancer of the prostate, breast, brain, etc.

Existing hyperthermia apparatus using ultrasound heats tumors to a moderate temperature of the order of 42.5° C. for a time of the order of one hour.

Since hyperthermia treatment may be insufficient, it can be advantageous to attempt to obtain much higher temperatures, for example of around 80° C., with a view to sensitizing cells or completely destroying them. To achieve this, it is necessary to supply acoustic energy to the tissue over a brief period, generally of the order of a few seconds, in order, notably, to avoid heat loss by natural transfer, notably due to blood circulation, throughout the tissue. Sufficient energy needs to be used and this implies using high ultrasound intensity.

This however brings one up against the technical problems resulting from cavitation phenomena which become even more accentuated as acoustic intensity increases, as has been described in detail by K. Hynynen in "The threshold for thermally significant cavitation in dog's thigh muscle in vivo" published in Ultrasound In Medicine and Biology, vol. 17, No.2, pages 157–171, (1991).

Acoustic cavitation covers any physical phenomena involving the activity of bubbles or micro-bubbles of gas undergoing movement as a result of an acoustic field.

Two types of cavitation can generally be distinguished:

stable cavitation where the walls of the bubbles are oscillating at the frequency of the ultrasound field without too great a consequence for the surrounding cells, but which considerably disturbs ultrasound transmission by reflecting or scattering incident waves. This phenomenon can appear at very low pressure levels as soon as bubbles are present in the medium;

transitory cavitation where bubbles expand up to their resonant size, and than implode violently. In this case, the energy accumulated by the bubbles is simultaneously released in the form of a shock wave, with intense heat (generally from 1000° to 20000° K) and microjets that can reach speeds of 100 m/s. All this leads to the creation of free radicals and mechanical destruction of surrounding tissue. Generally, this phenomenon appears starting from high incident pressures which thus defines the cavitation threshold.

Every living medium contains a certain amount of dissolved gas present in the form of bubble micronuclei Under the effect of an ultrasound field, the nuclei expand through a physical phenomenon known as rectified diffusion to reach a critical size known as the Blake threshold.

The inventor showed a while ago in an article entitled "Effects of cavitation in high intensity therapeutic ultrasound" published on pages 1357 to 1360 of volume 2 (1991) of "Ultrasonics Symposium Proceedings" (published by B. R. McAvoy) that the use of intensities that were too high, generally above 3000 W/cm^2 reduced the therapeutic effects of thermal treatment involving tissue destruction. This phenomenon can be explained by supposing that at these intensities, cavitation bubbles which may appear ahead of the focal spot act as a screen for incident ultrasound waves. Moreover, with the specific aim of reducing cavitation effects, F. J. Fry stated in International Patent application WO-A-89/07909 that it is necessary to inhibit production of micro-bubbles in the primary focal site to avoid lesions appearing outside said site (see page 15 of said Patent application). Under these conditions, it is stated that the intensity should not exceed 300 W/cm^2 at a 1 MHz frequency, or 2.100 W/cm^2 at 4 MHz.

K. Hynynen also showed in the above-cited article that an intensity of 700 W/cm^2/MHz should be considered as a maximum value to be used in hyperthermia treatment as, at higher levels, cavitation leads to unpredictable energy absorption.

To sum up the state of the art, cavitation hinders penetration of acoustic waves into tissue thus preventing treatment from following predictable lines. Moreover, cavitation can lead to uncontrolled tissue destruction, outside the target volume. It is thus appropriate, regardless of the application envisaged (in other words thermal treatment at high temperature for tissue destruction, or at moderate temperature or hyperthermia), to increase cavitation onset thresholds.

To avoid cavitation, the only recommendations that can be found in the prior art consist either in reducing acoustic intensity, or emitting in a discontinuous manner, using wave trains of determined duration, and respecting a waiting time between the trains, or, yet again, increasing emission frequency.

However, reducing acoustic intensity or using discontinuous emission leads to a loss of acoustic energy transmitted to the medium, which limits temperature rise or increases treatment duration. Furthermore, increasing emission frequency limits the depth of treatment, absorption by tissue being directly proportional to frequency, as described by Daniels et al., in the journal "Ultrasound in Medicine and Biology" vol. 13, No.9, (1987) in the article entitled "Ultrasonically induced gas bubble production in agar based gels". It should also be noted that, in the prior art, continuous sinewaves are employed for tissue heating, and thus emission duration is far higher than signal period. Usually, insonification of tissue for several seconds at a frequency comprised between 1 and 5 MHz is envisaged.

Certain authors have, on the other hand, considered using acoustic waves of a pulsed type, with a duration of the order of several periods, in other words several microseconds, but

for a completely different purpose, specifically either the destruction of concretions (lithotritation), or for diagnosis (Doppler ultrasound scanning).

The cavitation phenomena produced by such pulses have been studied. For example, Fowlkes and Crum in an article entitled "Cavitation threshold measurements for microsecond length pulses of ultrasound" published in J. Acoustic Soc. Am. 83 (6), June 1988, investigates the evolution of cavitation threshold as a function of pulse width and pulse frequency. Similarly, Delius, while studying cavitation produced by lithotripters recommended reducing acoustic wave repetition rates (see "Effects of lithotripter shock waves on tissue and materials", Frontiers on non-linear acoustics, edited by M. F. Hamilton and D. T. Blackstock, Elsevier Science Publishers, London 1990).

However, pulse methods do not make it possible to produce a temperature rise in tissue since each pulse only transports small amount of energy, and the pulses need to be spaced. It is thus not possible to assimilate work done with these waves with the work at the basis of this present invention.

SUMMARY OF THE INVENTION

Thus, the principle aim of the present invention is to resolve the new technical problem of providing a solution enabling maximum energy to be supplied to the medium, preferably the tissue of a living being, in particular an animal or human being, in the shortest possible time and preferably reducing or preventing the occurrence of cavitation phenomena.

A further aim or the invention is to resolve the new technical problem of providing a solution enabling maximum energy to be supplied to the medium, preferably the tissue of a living being, in particular an animal or human being, in the shortest possible time, while simultaneously ensuring safe and effective control of heat deposit, thus making it possible either to provide moderate thermal treatment in the framework of hyperthermia, or to carry out thermal treatment at high temperatures to achieve tissue destruction, preferably reducing or limiting cavitation phenomena.

Moreover, the invention resolves the new problem of secondary focusing which can occur when periodic or quasi-periodic structures are present on the path between the emission device and the region to be treated.

The present invention has the further aim of resolving the above technical problems in a simple, reliable, inexpensive manner making widespread industrial and medical use possible.

The present invention provides a satisfactory solution for the first time to the technical problems defined above, and has further technical advantages which will become more clear from the detailed description which follows, including the attached drawings which constitute an integral part thereof.

Thus, according to a first aspect, there is provided a method for generating ultrasound waves in a propagation medium comprising activating at least one ultrasound transducer element by an electronic signal supplied by a signal generator and reducing or preventing cavitation phenomena resulting from the propagation of ultrasound waves emitted by the ultrasound transducer element within the propagation medium by the use of a signal generator supplying a wideband electronic signal.

In this invention, in other words in the description and claims, the expression "wideband" for the spectrum of an electronic signal means that signal spectrum bandwidth is about 50% of the central frequency. For example, for a signal of central frequency 2 MHz, the bandwidth will be around 1 MHz and will thus cover frequencies varying from about 1.5 MHz to about 2.5 MHz.

In a preferred embodiment, a signal generator supplying a continuous random or pseudo-random electronic signal is employed.

Throughout this specification, the term "continuous" should be taken to mean that the duration of emission of the signal is very much longer than the period of the signal, as has already been said in the introduction above.

According to one preferred feature, the abovesaid signal generator supplies a pseudo-random electronic signal of the Gaussian or Poissonian distribution type. Such signal can typically be obtained from a source of thermal noise amplified by electronic amplification.

According to a further advantageous feature, the signal generator supplies a pseudo-random electronic signal using Golay coding.

According to a further advantageous feature, the signal generator supplies a pseudo-random electronic signal using Barker coding.

According to still a further advantageous feature of the invention, the signal generator supplies a coded electronic signal of M-sequence pseudo-random type.

M-sequence signals also referred to as maximum length binary sequences are of the type described by Jean-Yves Chapelon in Chapter 6, on pages 225 to 236, particularly page 230 onwards of the book "Progress in medical imaging" edited by Professor Newhouse and published by Springer Verlag, New York, 1988 which is incorporated herein by reference.

Such M-sequence or Golay or Barker pseudo-random coded signals can be employed directly or can phase- or frequency-modulate an electronic signal the carrier frequency of which corresponds to the transducer's nominal operating frequency.

Coded signals of the M-sequence pseudo-random type are particularly preferred. Such signals are precisely described in "Progress in medical imaging". Briefly, they consist of binary signals built up by pseudo-random repetition of pulses of elementary duration. Each of said sequences is repeated with a repetition period T that is characteristic of the M sequence.

A more precise description of an M sequence signal can be provided with reference to FIG. 4 attached:

- elementary pulse duration "θ"0.1 μs<θ<100 μs, ideally about 1 μs,
- repetition period T: 1 μs<T<10 s, ideally comprised between 0.5 and 5 s.

The pseudo-random type coded signals, particularly the currently preferred M sequence pseudo-random type signals can readily be obtained using electronic circuits well known to those skilled in the art.

The use of such wideband electronic signals, preferably random or pseudo-random, makes it possible to achieve better control of heat deposition and to avoid temperature increase disturbance by secondary effects such as cavitation, thus enabling spontaneous tissue destruction to be avoided particularly in the case of moderate heating used in hyperthermia.

Secondly, considering high-intensity use, the invention makes it possible to employ higher intensities and to reduce, for a given ultrasound dose, firing duration and,

consequently, the duration of treatment, while avoiding cavitation phenomena thus making it possible to carry out treatment of tumors in living beings, in particular animals or human beings, with higher level of safety while reducing the risk of damage at various interfaces.

From a second aspect, the present invention also provides a therapy apparatus comprising an actual therapy device including at least one ultrasound therapy transducer element and a signal generator supplying an electronic signal to said ultrasound transducer element, in which the signal generator supplies a wideband electronic signal of the random or pseudo-random type.

In one preferred embodiment, the signal generator supplies a Gaussian or Poissonian distribution type random signal.

In another preferred embodiment, the signal generator supplies a Golay coded or a Barker coded pseudo-random signal.

In another preferred embodiment, the signal generator supplies an M-sequence pseudo-random type coded electronic signal.

This M-sequence pseudo-random type coded electronic signal preferably has an elementary pulse duration (θ) theta comprised between 0.1 μs and 100 μs and is ideally of about 1 μs, and a period of repetition T about between 1 μs and 10 s and ideally about between 0.5 s and 5 s.

In either aspect of the invention, to increase the effectiveness of cavity effect reduction or prevention, an ultrasound transducer which preferably is itself wideband, is used, in other words the ultrasound transducer generates ultrasound waves when excited by a signal the frequency of which is substantially different from its nominal frequency.

Usually, two types of transducer can be used for generating continuous ultrasound waves for therapeutic purposes. These comprise, firstly, conventional ultrasound transducers essentially consisting of piezoelectric ceramic. Such ceramics have an acoustic impedance which is very different from that of the propagation medium and, as a result of this, their coupling with said medium is poor. This results in strong vibrations of the ceramic when it is excited by an electric signal, the resulting ultrasound transducer having a narrow frequency bandwidth.

For therapy carried out to date using ultrasound waves, such transducers are suitable as the control signals are themselves of the narrow band type.

In the framework of this invention, the frequency band of the ultrasound transducers is widened by the application of different types of treatment to the ceramic surface, these modifying ultrasound coupling with the propagation medium. Particularly, a layer of materials having an acoustic impedance intermediate between that of ceramic and the propagation medium of appropriate thickness is deposited in this case on the ceramic, such a layer being referred to as a quarter-wave layer. A so-called backing layer could also be deposited on the back of the ceramic between the latter and the air. These two types of treatment of the ceramic enable a wideband ultrasound transducer to be obtained.

Another type of wideband transducer can be obtained using composite type materials, this being particularly suitable for implementation in the present invention for reducing or preventing cavitation effects.

This makes it possible to obtain the determining technical advantages stated above.

According to a further aspect, the invention discloses the use, in a therapy apparatus including at least one ultrasound transducer and a signal generator supplying an electronic signal to said transducer, of a wideband electronic signal for reducing or preventing secondary focusing phenomena behind a periodic or quasi-periodic structure.

This for example makes it possible to treat the liver behind the rib cage by reducing or preventing lesions due to secondary focusing or side lobe phenomena.

In one embodiment of this third aspect of the invention, the wideband electronic signal is of the random or pseudo-random type.

The wideband electronic signal can be a Gaussian or Poissonian distribution type random signal.

The wideband electronic signal can also be a Barker coded or Golay coded pseudo-random signal.

For the wideband electronic signal, one can use a M-sequence pseudo-random type coded electronic signal of a frequency having an elementary pulse duration of about between 0.1 μs and 100 μs and ideally of about 1 μs, and a period of repetition T of about between 1 μs and 10 s and ideally of about between 0.5 s and 5 s.

The electronic wideband signal may also have an autocorrelation function approaching a Dirac function.

Further characteristics of the invention will become clear from the detailed description that follows, including the drawings which constitute an integral part thereof and the claims accompanying this description.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be described on the basis of a currently preferred embodiment thereof simply by way of illustration which in no manner should be considered as limiting the scope on the invention, with reference to the attached drawings.

FIG. 1 is a highly schematic representation of a known therapy device for performing therapy of the tissue of a living being, including a single- or multi-transducer device having one or several piezoelectric transducers, in the form of a semi-spherical cup allowing geometrical focusing on the propagation axis visible in FIG. 2;

FIG. 2 shows a curve in the form of a sinewave as a function of time t on the x-axis and amplitude A on the y-axis, according to the prior art as employed in an ultrasound wave generating device of FIG. 1;

FIG. 3 is a highly schematic view of a therapy device according to the present invention for carrying out therapy of living being tissue, including a wideband electronic signal generating device, said signal being preferably random or pseudo-random, delivered to the piezoelectric transducer device for generating an ultrasound wave, the random or pseudo-random signal being shown diagrammatically in FIG. 3, and in detail in FIG. 4 as a function of time expressed in microseconds on the x-axis, with amplitude on the y-axis;

FIG. 5 is a block diagram of a setup making it possible to clearly bring to light reduction in cavitation by using a random or pseudo-random type electronic signal for exciting the ultrasound transducer;

FIG. 6 shows results obtained with the apparatus in FIG. 5 in the form of a graph in which the line identified by the reference 2 corresponds to the random or pseudo-random signal according to the invention of FIGS. 3 and 4 joining the points shown by the -•- signs, and the line bearing the reference 1 results from the use of a sinewave signal according to the prior art employed in FIGS. 1 and 2, and joining the points -•-, as a function of power transmitted by the transducer expressed in Watts on the x-axis, the value in nanoamperes provided by an ammeter integrating the total amount of light emitted by the luminol employed being indicated on the y-axis;

FIG. 7 shows schematically the operation of a prior art device in the presence of a periodic or quasi-periodic structure; and

FIG. 8 is a schematic representation similar to that in FIG. 7 in a device implementing the invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENT

With reference to FIG. 1, there is shown diagrammatically a known therapy device generally identified by reference numeral **10**, for carrying out therapy of the tissue of a living being.

This therapy apparatus **10** includes an actual therapy device which here takes the form of a semispherical cup **22** using natural focusing including one or several piezoelectric transducer elements, in particular a single-element piezoelectric transducer identified by reference **23** having substantially the same dimensions as the semi-spherical cup **22** as is well known to those skilled in the art, no supplementary description thereof appearing necessary. One example of an embodiment of such a therapy device is, for example, one in the form of a semi-spherical cup **22** of 100 mm diameter, using natural focusing at a focal length of 100 mm, with an operating frequency of about 1 MHz, using one single piezoelectric transducer element **23**.

Transducer element **23** is linked, via an amplifier device **30**, to a signal generator **40** which can itself be controlled by a control unit **50**.

It should be noted that, in accordance with another possible embodiment, semi-spherical cup **22** using natural focusing can be subdivided into an annular array, well known to those skilled in the art, or into a mosaic also known to those skilled in the art, and no supplementary description thereof appears necessary. In this case, each individual annular or mosaic-like transducer element is linked via an amplifier device including individual amplifiers and a delay-line device including individual delay lines, to a common signal generator such as signal generator **40** controlled in its turn by control unit such as control unit **50**. The control unit then controls the delay lines by supplying the delay value needed by each line for obtaining focusing at the desired focal length.

Due to this design of the apparatus, dynamic electronic focusing with focal length being varied at will can be achieved.

Considering the prior art apparatus of FIG. 1, when a conventional electronic signal is generated by generator **40** of the sinewave type as shown schematically at the output from amplifier **30** and, in more detail, in FIG. 2, for example at a frequency of around 1 MHz, natural focusing is obtained in the focal region F defining the treatment volume T.V.

With such a continuous sinewave signal, in other words one having a duration distinctly higher than the frequency value per period, which in general is several seconds compared to a 1 MHz frequency, bubbles of gas present in tissue or which are spontaneously generated by ultrasound waves, identified by reference B, which are present ahead of the various interfaces, for example of focal region F or the interface with the skin S of the patient P, will start oscillating after several pulses at frequency f_p, called the pumping frequency. The diameter of the gas bubbles B will increase at each pulse due to the so-called rectified diffusion phenomenon, to reach a maximum value that is characteristic of the frequency f_p, or Blake threshold. When the acoustic field intensity exceeds the cavitation threshold, which practically always is the case in therapeutic treatment, the bubbles will implode releasing energy. This cavitation threshold is identified by the general reference character C on FIG. 2 for sinewave signal intensities of relatively high amplitude.

This constitutes a major disadvantage in the state of the art.

Under these conditions, and with reference to FIG. 3, an apparatus according to the present invention is shown generally identified by reference numeral **100**. The same reference numerals increased by **100** have been used to identify those parts that are identical, or operate identically, to those in the prior art apparatus. Thus, the actual therapy device is here identified by the reference **120**, the semi-spherical cup by **122** and the piezoelectric transducer element by **123**, the amplifier device by **130** and the electronic signal generator device and control unit by **140** and **150** respectively.

In the framework of the apparatus according to the invention, the signal generator device **140** supplies a wideband electronic signal, identified by the reference A.S. shown on FIG. 3, at the output from amplifier device **130**, this being shown in more detail on FIG. 4.

For this invention, the ultrasound transducer can itself be a wideband device, implemented as described previously.

In the invention and for providing an endorectal probe for prostate treatment, it is preferred to use a transducer in the form of a semi-spherical cup of about 35 mm diameter using natural focusing at the focal length of 35 mm, while, preferably, a signal having a central frequency of about 2.25 MHz is employed.

As has been said above, the term wideband spectrum in this present description and claims should be taken to mean that the bandwidth of the signal spectrum is about 50% of the central frequency. For example, for a signal having a central frequency of 2 MHz, bandwidth will be about 1 MHz and will thus comprise frequencies from about 1.5 MHz to about 2.5 MHz.

In the invention, more particularly for the purpose of reducing or preventing cavitation phenomena resulting from the propagation of ultrasound waves emitted by the ultrasound transducer element **123** in the propagation medium PM1, PM2, signal generator **140** supplies a random or pseudo-random wideband electronic signal, identified by reference A.S. in FIGS. 3 and 4. The central frequency is generally comprised between 20 MHz and 0.5 MHz.

It will be noted that, in the framework of the invention, the use of random or pseudo-random signals provides an excitation ultrasound field spectrum consisting of a multiple-frequency spectrum, the random appearance characteristic of which limits bubble growth, so that the latter rarely attain the critical diameter above which cavitation effects occur.

Thus, the invention makes it possible to limit or prevent cavitation phenomena.

The random or pseudo-random signal supplied by signal generator **140** is of the type described above and can, for example, be a Golay or Barker coded pseudo-random electronic signal, these being well known to those skilled in the art, particularly from the preceding description.

An M-sequence pseudo-random coded electronic signal can also be employed, this preferably having an elementary pulse duration (θ) theta, about between 0.1 μs and 100 μs, and a repetition period T about between 1 μs and 10 s.

A random signal of a Gaussian or Poissonian distribution type can also be employed.

It should be noted that the electronic signal shown in FIG. 3 and in detail in FIG. 4 is an M-sequence pseudo-random

electronic signal the period of which T is comprised between 1 μs and 10 s the elementary pulse duration theta (θ) being about between 0.1 μs and 100 μs.

With reference to FIG. 5, there is here shown an apparatus making it possible to demonstrate reduction in cavitation when electronic signals, or pseudo-random codes according to the present invention are employed, is thanks to the use of a luminol. This chemical compound is known to emit photons (fluorescence) when in the presence of cavitation, as described in the article by Fowlkes et al. in J. Acoust Soc. Am. vol. 83 of June 88 page 2190–2200 entitled "Cavitation threshold measurements for microsecond length pulses of ultrasound".

This apparatus includes, in the schematic form of FIG. 5, a frequency generator **160** associated with a code generator **170**, the combination of the two generators **160** and **170** corresponding to the electronic signal generator **140** of FIG. 3, coupled to an amplifier device **130** for supplying a pseudo-random or random type electronic signal according to the present invention, for example an M-sequence signal, to transducer element **123** placed in a tank **180** containing a solution of luminol **182**. In the luminol solution **182**, not only is transducer **123** immersed, but a photomultiplier **184** device is also present, connected to a moving-needle nanoammeter **186** providing a measurement in nanoamperes proportional to the photoluminescence obtained using the luminol.

The luminol solution **182** is obtained from a solution of demineralized distilled water, saturated with air at atmospheric pressure, and of luminol (aminophtalhydrazide, 1.4 mmol previously dissolved in hplc-grade dimethylsulfoxide (DMSO)). The solution was buffered with CAPS (3-cyclohexylamino 1-propane sulfonic acid), 25 mmol and balanced to a pH of **10** with 0.1M soda.

For this experiment, the ultrasound transducer element **123** employed had a diameter of 5 cm, and focused to 97 mm. The tank was a cylindrical 40 ml container arranged horizontally, with a length of 5 cm in which focusing effects did not participate, the energy being distributed throughout the tank. Transducer resonant frequency was 1.11 MHz, said value being obtained at the sonoluminescence maximum of the water.

The photomultiplier is for example Hamamatsu type R374 comprising a lens optical system for receiving the fluorescence emitted by the luminol. Tank **180** was optically isolated to avoid any light interference. Photomultiplier **184** was powered by a small generator not shown here and the light signal was read on the ammeter **186** that integrated the total amount of light emitted by the luminol.

Transducer **123** was connected to power amplifier **130**, which, for example, is of the Ampar 801, Prana, having a passband ranging from 0.1 to 1.8 MHz. The electronic signal or M-sequence pseudo-random code generator was manufactured by the INSERM having a period T of about 60 ms, and an individual pulse duration (θ) of 1.8 μs, and was synchronized by a HP 8116 A type function generator. Wattmeter **132** was a Rhode & Schwarz digital wattmeter reference NAP which allowed incident and reflected power to be measured.

Regarding wattmeter **132** readings, the references indicated on FIG. **5** have the following meanings:

"PdNC"=direct power from an uncoded signal, in other words a sinewave signal of the prior art;

PrNS"=reflected power from an uncoded signal, in other words a sinewave signal of the prior art;

"PdC"=direct power from a coded signal, in other words a random or pseudo-random type signal of the invention;

"PrC"=power reflected with a coded signal, in other words a random or pseudo-random type signal of the invention.

Measurement were made at different powers, firstly with an uncoded signal (NC) (monochromatic signal at 1.11 MHz) or continuous sinewave of the prior art, such as signal S_1 of FIGS. 1 and 2, which enabled line 1 to be obtained shown by the circles or dots in FIG. 6 for comparative purposes. Secondly, this same signal modulated with a pseudo-random code made it possible to obtain an M-sequence pseudo-random electronic signal according to the invention, as shown in FIGS. 3 and 4 bearing the reference AS, which provided the line 2 identified by the diamond-shaped points on FIG. 6.

In both cases, the signal generated was maintained until a luminescence plateau was achieved. The solution was injected into the tank manually with a 50 ml syringe, this always being done in the same way.

For each power tested, measurement was repeated 4 times with the same solution. Between these four measurements, the solution was drawn off from the tank and reinjected in order to maintain a constant degree of saturation. On the other hand however, when there was a change from one power to the other, the solution was thrown away and renewed.

Temperature was relatively stable (23°–28° C.), radiation time being short and the transducer being only cooled from the back with a cold water circuit (not shown) on its metal part.

The results obtained are given in table I below.

V_{in} (mV) is the input voltage at the Prana type power amplifier **130**. P_d and P_r are, respectively, the direct and reflected powers read on wattmeter **132**, P_{Trans} being the power transmitted by the transducer ($P_{Trans}=P_d-P_r$). Lum is the luminescence value read on nanoammeter **186**. The indices C and NC respectively characterize a random or pseudo-random (A.S.) type coded signal according to the invention (FIGS. 3 and 4) and an uncoded signal, in other words an S1-type sinewave according to the prior art (FIGS. 1 and 2).

The luminescence values obtained from a signal coded according to the invention are shown by line 2 with diamond-shaped points in FIG. 6, line 1 joining the circles or dots giving the figures for a sinewave uncoded signal according to the prior art in FIG. 6, as a function of signal power transmitted by the transducer, in Watts. For values below 10 W, the luminescence measured for the two signals corresponds to the natural luminescence of water.

The cavitation threshold was obtained around 12 to 15 W for the uncoded signal of the continuous sinewave type of the prior art whereas this was never reached in the range of power employed with random or pseudo-random type coded signal according to the present invention.

It was not possible to make measurements above 40 W without putting the ultrasound transducer **123** at risk.

Vin (mV)	PdNc (W)	PrNc (W)	PdC (W)	PrC (W)	LumNC (nA)	LumC (nA)	P_{Trans}^{NC} (W)	P_{Trans}^{C} (W)
34	13,0	0,6	31,5	19,0	29	49	12,4	12,5
39	15,3	0,6	39,5	24,1	130	61	14,7	15,4
44	20,0	0,9	50,8	31,1	600	71	19,1	9,7
49	26,3	1,5	61,2	37,2	1400	78	24,8	24,0
55	32,1	1,7	77,0	47,0	2600	95	30,4	30,0
62	41,0	2,2	98,3	59,6	4325	89	38,8	38,7

Thus, it can be seen that, unexpectedly, by using a wideband electronic signal according to the present invention and, for example, a pseudo-random or random type coded electronic signal, no cavitation phenomena appear in the range of powers used for the experiment, this being reflected by the set of steady values for luminescence as a function of power, in contrast to line 1 obtained with a sinewave signal of the prior art.

This constitutes a surprising result of the present invention.

FIG. 7 is a highly schematic representation of the operation of a device according to the prior art, in the presence of a periodic or quasi-periodic structure; in FIG. 7, a therapy device **200** linked via an amplifier **203** to a signal generator **204** can be seen.

As mentioned above, the therapy device is for example a semi-spherical cup with natural focusing, comprising one or several transducer elements (a single transducer, or a set of annular or mosaic ceramic elements).

The therapy device sets up an ultrasound field **205** directed towards the treatment region **206**. A periodic or quasi-periodic structure **207** is disposed in the ultrasound field **205** between a therapy device **200** and the treatment region **206**, reference **210** identifying the focal spot. This structure can for example be the rib cage, in the case of external treatment of tumors of the liver.

In devices of the prior art driven by a conventional sinewave type signal or, more generally, excited by periodic signals, such a periodic structure leads to the appearance of secondary points of focus **208**, **209** (or side lobes) outside the treatment region as a result of diffraction of the ultrasound waves passing through structure **207**. The appearance of such secondary points of focus has obvious consequences for the safety of treatment. Moreover, radiation of energy to these secondary points decreases the power radiated to focal point **210**, and can compromise the effectiveness of treatment. One can say that in this configuration, secondary focusing phenomena occur behind the periodic or quasi-periodic structure. In this specification, the expression "behind the periodic or quasi-periodic structure **207**" should be taken to mean "downstream, regarding the propagation path of ultrasound waves, of the periodic or quasi-periodic structure **207**".

FIG. 8 shows the same arrangement as in FIG. 7 in a device implementing the invention. The invention discloses the use of a signal generator supplying a wideband electronic signal for exciting the therapy device. As described above, the signal generator may supply a random or pseudo-random electronic signal and, more particularly, a Golay or Barker coded pseudo-random electronic signal or an M-sequence pseudo-random coded type electronic signal (of the type described above for example).

The invention can also be characterized in that the therapy device is excited by a signal having an auto-correlation function that is as close as possible to a Dirac function. The signals above have an auto-correlation function which approaches that of a Dirac function.

FIG. 8 illustrates the results of the invention: the secondary points of focus caused by the periodic or quasi-periodic structure have disappeared; the position of such focal points does in fact essentially depend on the periodicity of the structure **207** and the ultrasound frequency. The use of wideband signals causes the position of the secondary point of focus to vary during the course of treatment. In this way, there is no longer a local build-up of energy outside the treatment region in the area surrounding the principal point of focus **210**. The invention thus makes it possible to decrease the risk of producing secondary lesions outside the treatment region, even in the presence of a periodic or quasi-periodic structure.

The invention makes it possible to achieve accurate and localised treatment, even behind a periodic or quasi-periodic structure such as, for example, treatment of the liver behind the rib cage.

The various embodiments of the invention described with reference to the preceding figures can obviously be combined.

The present invention obviously includes all means constituting technical equivalents of the means described, as well as various combinations thereof.

Moreover, FIGS. 3 to 6 constitute an integral part of this invention and thus of the description.

What is claimed is:

1. A method for generating high power therapeutic ultrasound waves in a propagation medium, said ultrasound waves produced by an ultrasonic transducer having at least one ultrasound transducer element, the method comprising the steps of activating said at least one ultrasound transducer element with an electronic signal supplied by a signal generator, the signal generator supplying a wideband electronic signal to said at least one ultrasound transducer element, said wideband signal having a multiple frequency spectrum, the wideband signal configured to reduce or prevent cavitation phenomena resulting from the propagation of the ultrasound waves emitted by said at least one ultrasound transducer element within the propagation medium.

2. The method according to claim 1, wherein said signal generator is a signal generator supplying a random or pseudo-random electronic signal.

3. The method according to claim 1, wherein said signal generator is a signal generator supplies a Golay coded pseudo-random electronic signal.

4. The method according to claim 1, wherein said signal generator supplies a Barker coded pseudo-random electronic signal.

5. The method according to claim 1, wherein said signal generator supplies a M-sequence pseudo-random type coded electronic signal.

6. The method according to claim 5, wherein said M-sequence pseudo-random type coded electronic signal has an elementary pulse duration of about 1 μs and a period of repetition T of about between 0.5 and 5 s.

US006325769B1

(12) **United States Patent**
Klopotek

(10) **Patent No.: US 6,325,769 B1**
(45) **Date of Patent: *Dec. 4, 2001**

(54) **METHOD AND APPARATUS FOR THERAPEUTIC TREATMENT OF SKIN**

(75) Inventor: **Peter J. Klopotek**, Framingham, MA (US)

(73) Assignee: **Collapeutics, LLC**, Wellesley, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **09/340,997**

(22) Filed: **Jun. 28, 1999**

Related U.S. Application Data

(63) Continuation-in-part of application No. 08/998,963, filed on Dec. 29, 1998, now Pat. No. 6,113,559.

(51) **Int. Cl.**[7] **A61N 7/00**
(52) **U.S. Cl.** **601/2**
(58) **Field of Search** 601/2, 3, 4; 600/439; 604/20, 22; 606/27, 28, 31, 32

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,372,296	2/1983	Fahim	128/24
4,787,373	11/1988	Vogel	128/24.1
4,893,624	1/1990	Lele	128/399
4,938,216	7/1990	Lele	128/399
4,938,217	7/1990	Lele	128/399
4,960,109	10/1990	Lele	128/736
5,012,797 *	5/1991	Liang et al.	128/24
5,230,334	7/1993	Klopotek	128/399
5,413,550	5/1995	Castel	601/2
5,458,596	10/1995	Lax et al.	606/31
5,501,655	3/1996	Rolt et al.	601/3
5,507,790	4/1996	Weiss	607/100
5,569,242	10/1996	Lax et al.	606/42
5,618,275	4/1997	Bock	604/290
5,755,753	5/1998	Knowlton	607/98
5,810,801	9/1998	Anderson et al.	606/9
5,964,749	10/1999	Eckhouse et al.	606/9
5,983,900	11/1999	Clement et al.	128/898
6,113,559 *	9/2000	Klopotek	601/3

FOREIGN PATENT DOCUMENTS

2672486	8/1992	(FR) .
9108288	4/1997	(JP) .

OTHER PUBLICATIONS

Anvari, B. et al., "Cryogen Spray Cooling in Conjunction With Laser Treatment of Selected Dermatoses," 15th Annual Meeting of the American Society for Laser Medicine and Surgery, San Diego, CA, (Apr. 1995).

Anvari, B. et al., "Selective Cooling of Biological Tissues During Pulsed Laser Irradiation," 15th Annual Meeting of the American Society for Laser Medicine and Surgery, San Diego, CA, pp. 2–4 (Apr. 1995).

Bacon, D.R. and Shaw, A., "Experimental Validation of Predicted Temperature Rises in Tissue–Mimicking Materials," *Phys. Med. Biol.*, vol. 38, 1647–59 (1993).

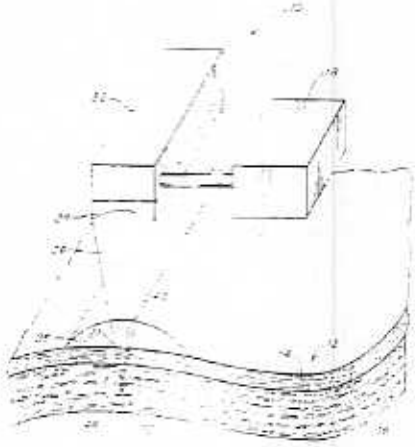
(List continued on next page.)

Primary Examiner—Marvin M. Lateef
Assistant Examiner—Eleni Mantus Mercader
(74) *Attorney, Agent, or Firm*—Thomas J. Engellenner; Tram Anh T. Nguyen; Nutter, McClennen & Fish, LLP

(57) **ABSTRACT**

A method and apparatus of reducing skin wrinkles, including applying an acoustic pulse or train of pulses to a subsurface region of human skin without damaging or adversely affecting the surface or epidermis layer of the skin. The pulses cause changes in the dermis layer of the skin that result in enhanced smoothness of the epidermis layer of the skin. In particular, the acoustic pulses are applied to the dermis layer at an amplitude and for a period of time sufficient to induce production of new connective tissue that reduces or eliminate of skin wrinkles.

41 Claims, 7 Drawing Sheets



OTHER PUBLICATIONS

Barnett, S.B. et al., "Current Status of Research on Biophysical Effects of Ultrasound," *Ultrasound in Med. & Biol.*, vol. 20, No. 3, 205–18 (1994).

Chandraratna, P. et al., "Characterization of Collagen by High–Frequency Ultrasound: Evidence for Different Acoustic Properties Based on Collagen Fiber Morphologic Characteristics," *Am. Heart J.*, vol. 133, 364–8 (1997).

Coleman, A.J. and Saunders, J.E., "A Review of the Physical Properties and Biological Effects of the High Amplitude Acoustic Fields Used in Extracorporeal Lithotripsy," *Ultrasonics*, vol. 31, No. 2, 75–89 (1993).

Crum, L.A. et al., "Acoustic Cavitation Produced by Microsecond Pulses of Ultrasound: A Discussion of Some Selected Results," *J. Acoust. Soc. Am.*, vol. 91, No. 2, 1113–9 (Feb. 1992).

Doukas, A. et al., "Biological Effects of Laser–Induced Shock Waves: Structural and Functional Cell Damage In Vitro," *Ultrasound in Med. & Biol.*, vol. 19, No. 2, 137–46 (1993).

Doukas, A., "Laser–generated Stress Waves in Medicine: From Tissue Injury to Drug Delivery," *OSA Trends in Optics and Photonics Series*, vol. 22, 312–6 (Mar. 8–11, 1998).

Doukas, A.G. and Flotte, T.J., "Physical Characteristics and Biological Effects of Laser–Induced Stress Waves," *Ultrasound in Med. & Biol.*, vol. 22, No. 2, 151–64 (1996).

Doukas, A. et al., "Physical Factors Involved in Stress–Wave–Induced Cell Injury: The Effect of Stress Gradient," *Ultrasound in Med. & Biol.*, vol. 21, No. 7, 961–7 (1995).

Enwemeka, C. et al., "The Biomechanical Effects of Low–Intensity Ultrasound on Healing Tendons," *Ultrasound in Med. & Biol.*, vol. 16, No. 8, 801–7 (1990).

Fan, X. and Hynynen, K., "Control of the Necrosed Tissue Volume During Noninvasive Ultrasound Surgery Using a 16–element Phased Array," *Med. Phys.*, vol. 22, No. 3, 297–306 (Mar. 1995).

Gelfand, J. et al., "Alterations in Body Temperature," In *Harrison's Principles of Internal Medicine*, Kurt J. Isselbacher et al., eds. (McGraw Hill), pp. 81–5, 2473–6 (1994).

Grundlagen, A., "Therapeutischer Ultrascha in der Tumortherapie," *Radiologe*, vol. 36, 64–71 (1996).

Lask, G. et al., "Nonablative Laser Treatment of Facial Rhytides," Conference 2870D, *Part of SPIE Proceedings. Cutaneous Applications of Lasers: Dermatology, Plastic Surgery and Tissue Welding*, vol. 2970, 1–12 (Feb. 9, 1997).

Miller, M. et al., "A Review of In Vitro Bioeffects of Inertial Ultrasonic Cavitation From a Mechanistic Perspective," *Ultrasound in Med. & Biol.*, vol. 22, No. 9, 1131–54 (1996).

Milner, T.E. et al., "Dymanic Cooling for Spatial Confinement of Laser Induced Thermal Damage in Collagen," 15th Annual Meeting of the American Society for Laser Medicine and Surgery, San Diego, CA, 2–4 (Apr. 1995).

Nyborg, W., "Scientifically Based Safety Criteria for Ultrasonography," *J. Ultrasound Med.*, vol. 11, 425–32 (1992).

Payne, P., "Measurement of Properties and Function of Skin," *Clin. Phys. Physiol. Meas.*, vol. 12, No. 2, 105–29 (1991).

Ramirez, A. et al., "The Effect of Ultrasound on Collagen Synthesis and Fibroblast Proliferation In Vitro," *Medicine and Science in Sports and Exercise*, 326–32 (1997).

Weaver, J. et al., "Mathematical Model of Skin Exposed to Thermal Radiation," *Aerospace Medicine*, 24–30 (Jan. 1969).

Webster, D.F. et al., "The Role of Cavitation in the In Vitro Stimulation of Protein Synthesis in Human Fibroblasts by Ultrasound," *Ultrasound in Med. & Biol.*, vol. 4, 343–51 (1978).

Webster, D.F. et al., "The Role of Ultrasound–Induced Cavitation in the "In Vitro" Stimulation of Collagen Synthesis in Human Fibroblasts," *Ultrasonics*, 33–7 (Jan. 1980).

* cited by examiner

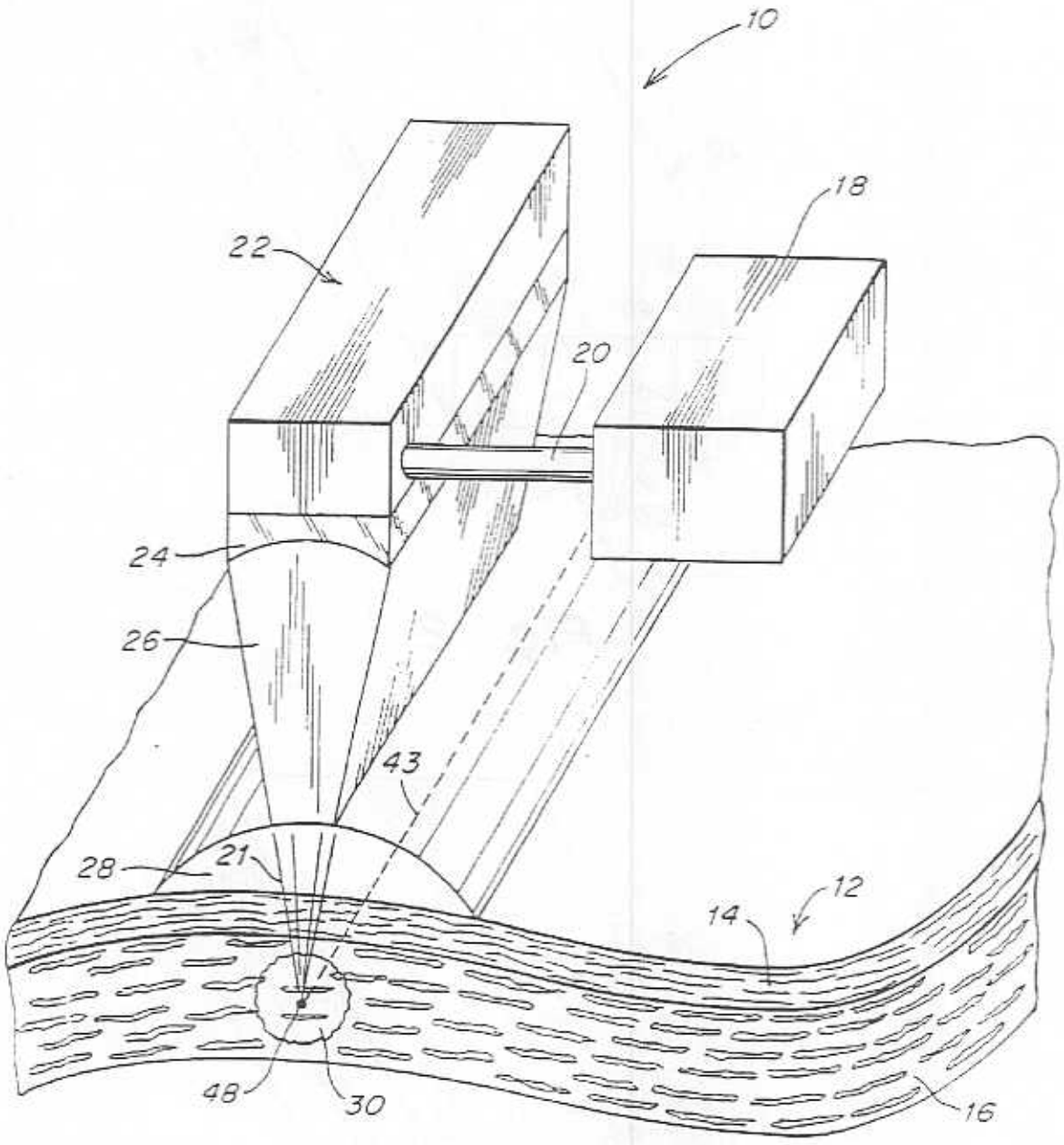


Fig. 1

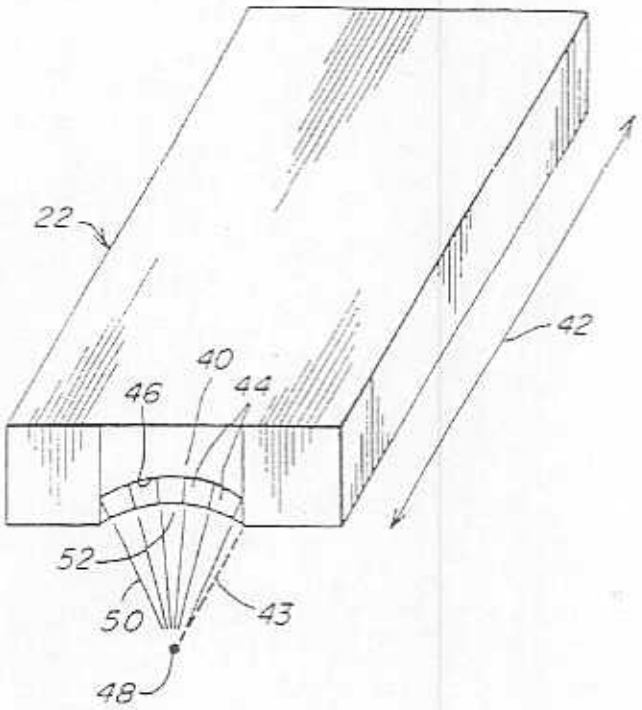


Fig. 2

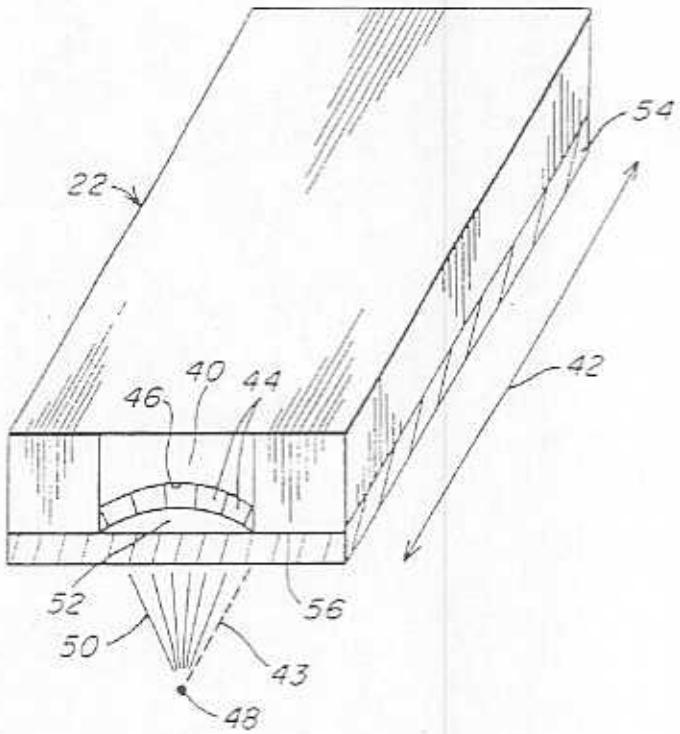


Fig. 3

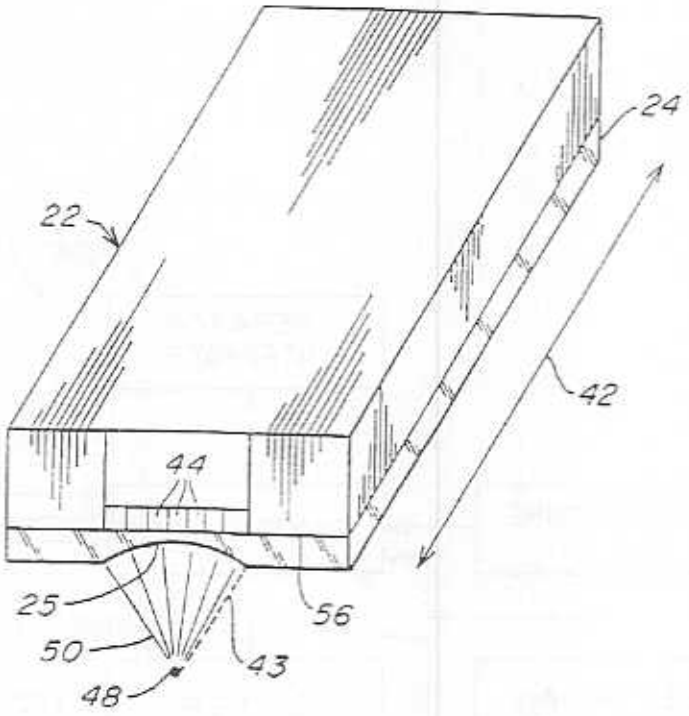


Fig. 4

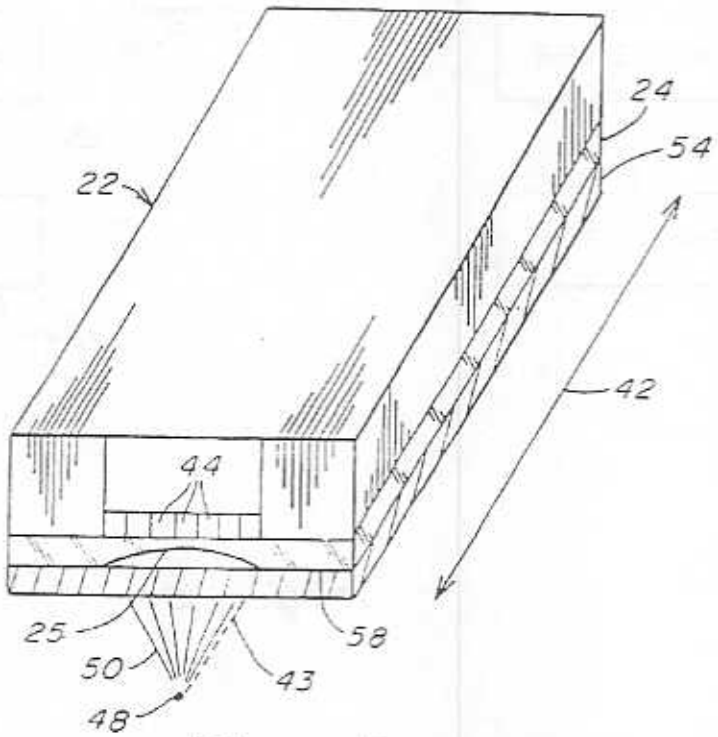


Fig. 5

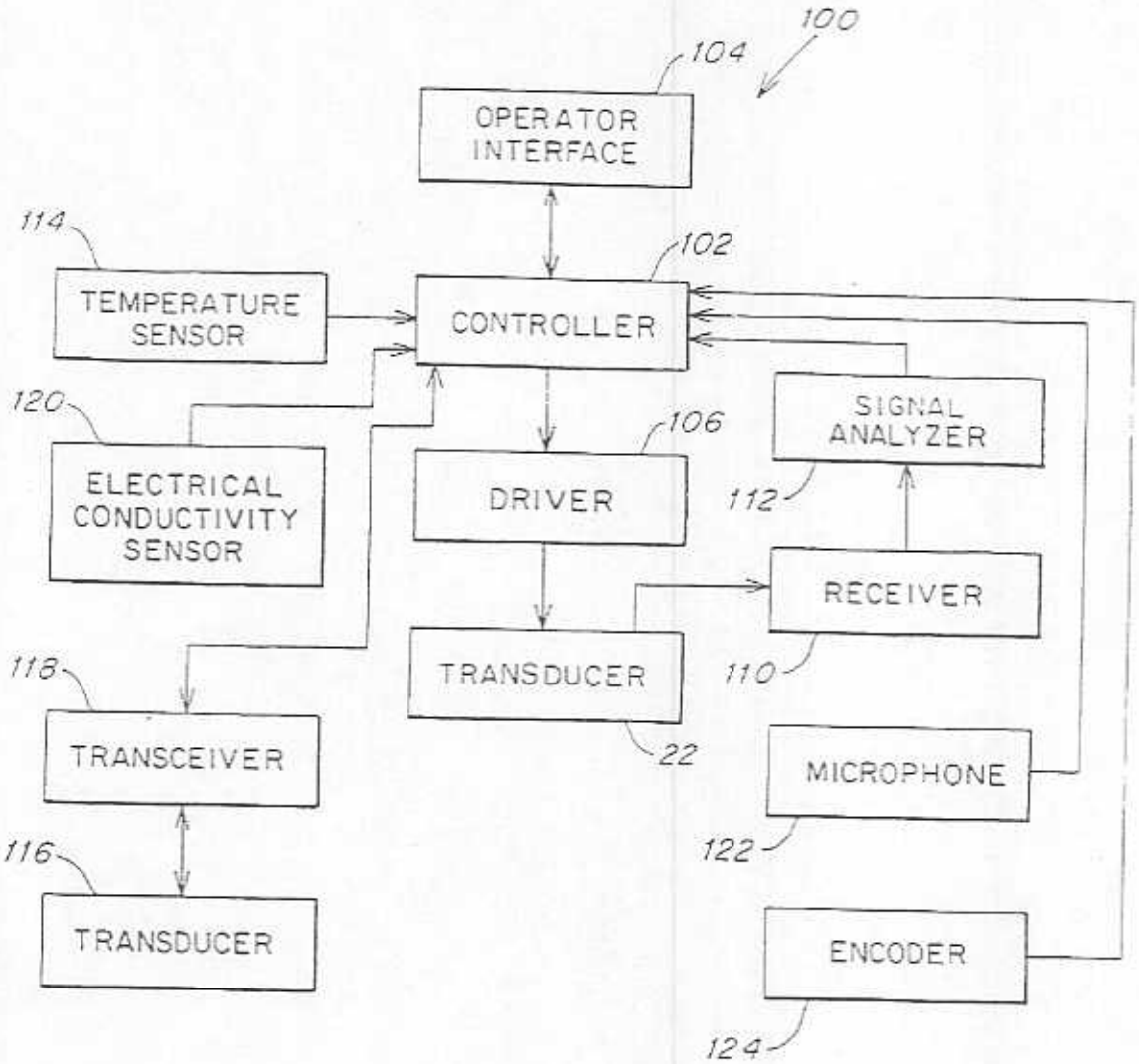

100
104
OPERATOR INTERFACE
114
TEMPERATURE SENSOR
102
CONTROLLER
120
ELECTRICAL CONDUCTIVITY SENSOR
106
DRIVER
SIGNAL ANALYZER
112
RECEIVER
118
TRANSCEIVER
TRANSDUCER
110
22
MICROPHONE
122
116
TRANSDUCER
ENCODER
124

Fig. 6

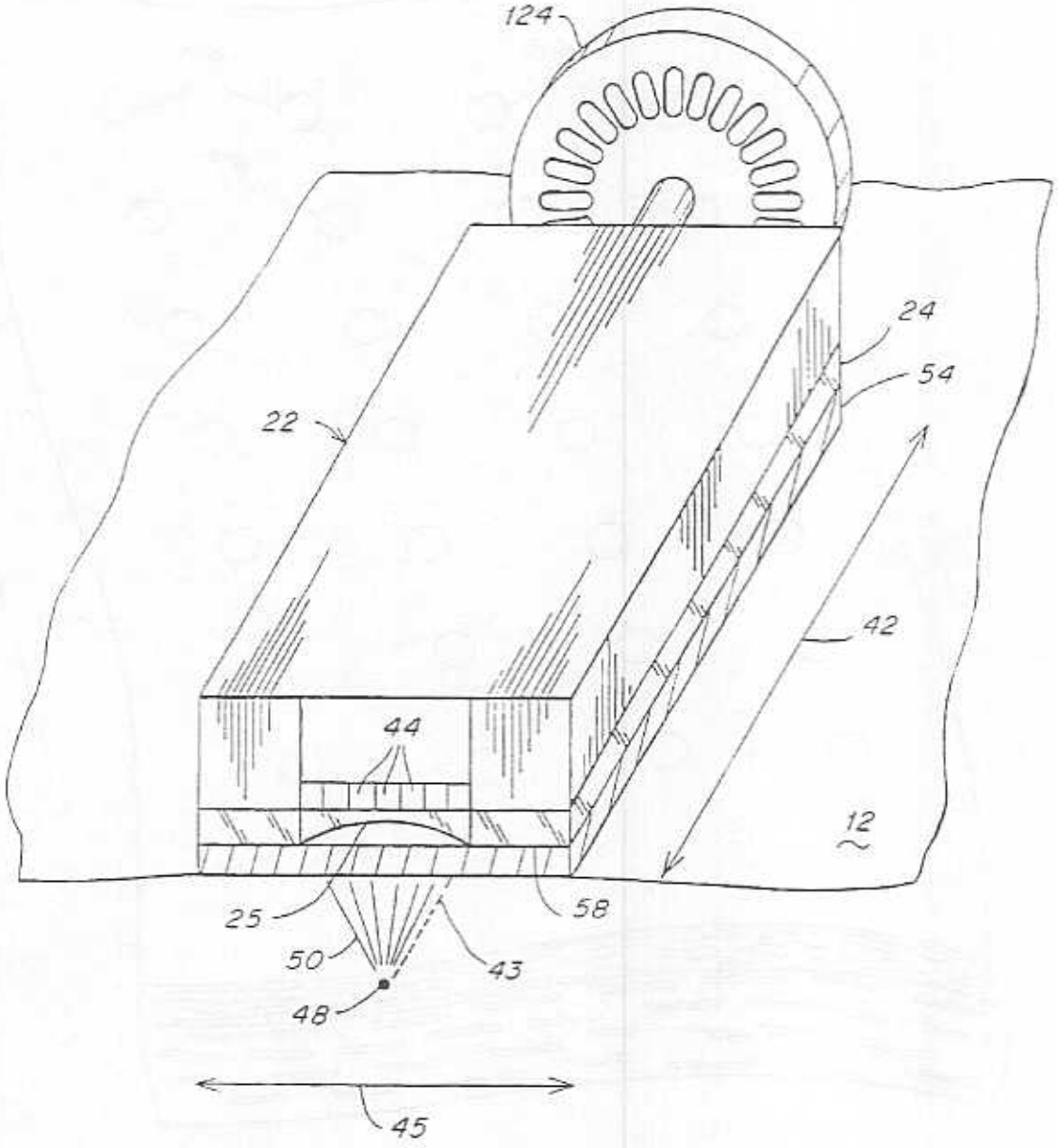


Fig. 7

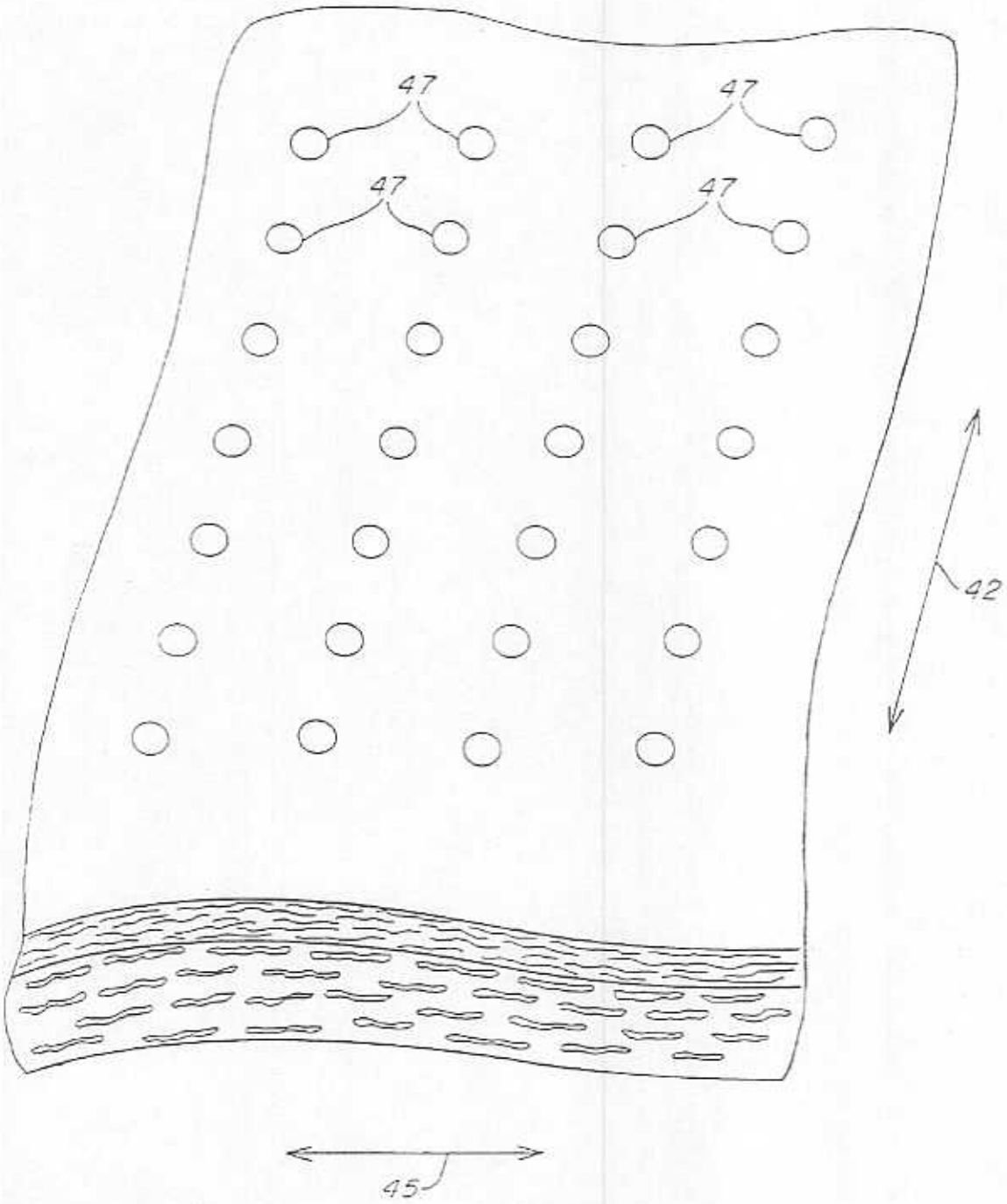


Fig. 8

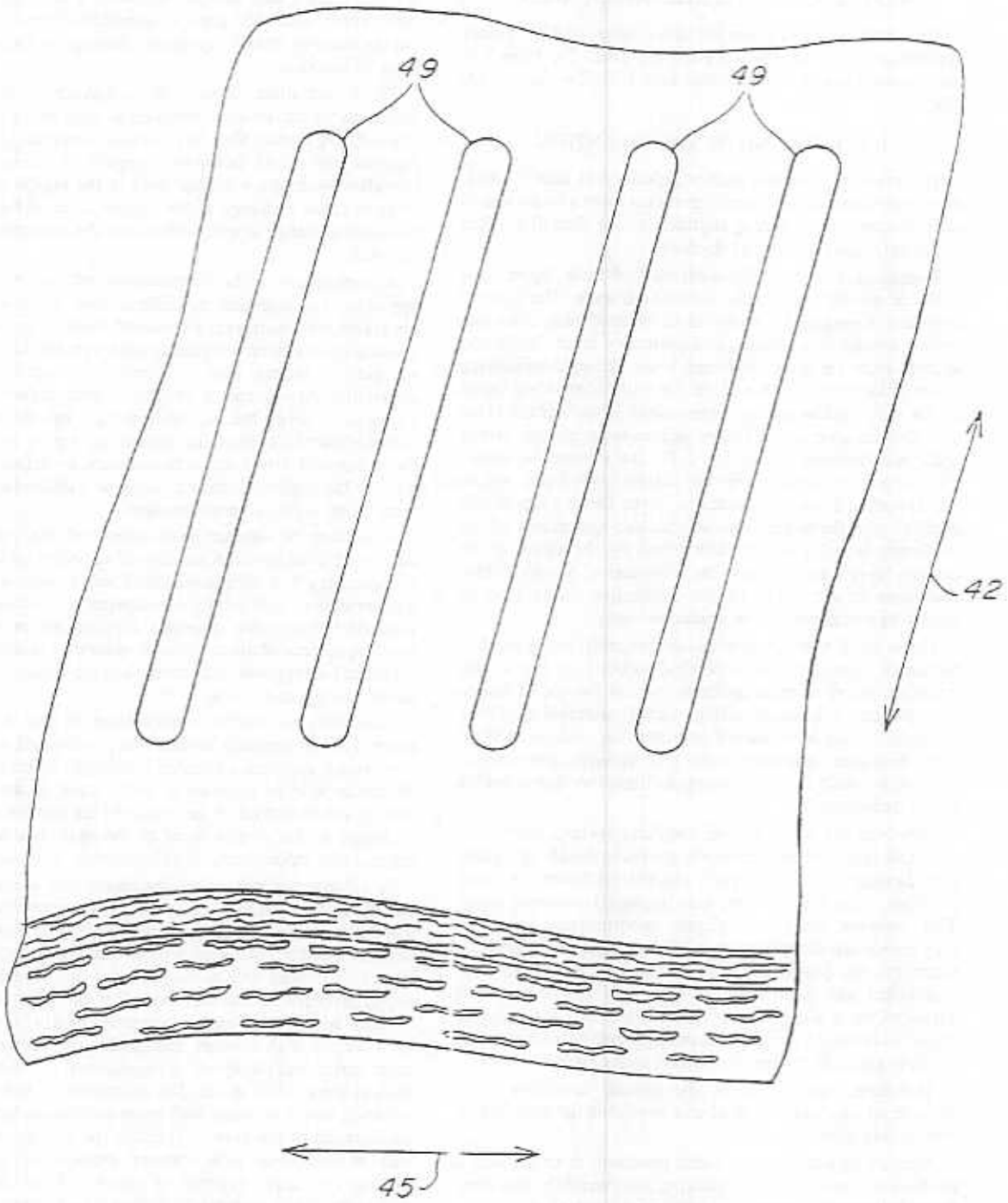


Fig. 9

METHOD AND APPARATUS FOR THERAPEUTIC TREATMENT OF SKIN

REFERENCE TO RELATED APPLICATION

This application is a continuation-in-part of U.S. patent application Ser. No. 08/998,963 filed Dec. 29, 1998 and incorporated herein by reference now U.S. Pat. No. 6,113,559.

BACKGROUND OF THE INVENTION

The present invention relates generally to skin therapy. More particularly, the present invention relates to the use of such therapy for reducing rhytides of the skin (i.e., skin wrinkles), especially facial rhytides.

Human skin is basically composed of three layers. The outer, or visible layer is the stratum corneum. The stratum corneum is essentially a thin layer of dead skin cells that serves, among other things, as a protective layer. Below the stratum corneum is the epidermis layer. The epidermis layer is a cellular structure that forms the outermost living tissue of the skin. Below the epidermis layer is the dermis layer that contains a variety of tissues such as sweat glands, nerves cells, hair follicles, living skin cells, and connective tissue. The connective tissue gives the dermis layer body, shape, and support. Since the epidermis layer lies on top of the dermis layer, the shape, smoothness, and appearance of the epidermis layer is in part determined by the shape of the dermis layer (and largely the connective tissue). Thus, variations in the shape of the connective tissue tend to appear as variations in the epidermis layer.

There are a number of methods currently being used to reduce or eliminate skin wrinkles, particularly facial skin wrinkles. Some of these methods include the use of lasers, cryo-peeling, chemical-peeling, and dermabrasion. These methods appear to stimulate or irritate the dermis layer so that a biological response results that produces new connective tissue which in turn reduces or eliminates skin wrinkles in the treated area.

However, the cryo-peeling, chemical-peeling, dermabrasion and laser ablation methods generally result in significant damage to the epidermis and dermis layers. In these methods, the epidermis layer may be peeled or burned away. This presents several problems: opportunistic infections may invade the dermis layer and thus complicate or prolong recovery; the procedure may cause a patient significant discomfort and pain; and the skin may appear raw and damaged for a significant period of time (on the order of weeks or months) while the healing process takes place. All of these side effects are considered undesirable.

Therefore, one object of the present invention is to provide an improved method and apparatus for reducing or eliminating skin wrinkles.

Another object of the present invention is to provide a method and apparatus for reducing skin wrinkles that does not substantially damage the epidermis layer of the skin.

SUMMARY OF THE INVENTION

The overall concept of the present invention relates to methods and apparatus for therapeutic treatment of skin using ultrasound. In particular, the present invention relates to wrinkle reduction and skin rejuvenation by controlled application of ultrasound energy into the dermis layer. The ultrasound energy triggers a biological response that causes synthesis of new connective tissue in the dermis through activation of fibroblast cells in the dermis without causing or requiring significant irritation or damage to the epidermis. One purpose of the present invention is to provide a cosmetic improvement in the appearance of the skin meaning that the treated skin surface will have a smoother, rejuvenated appearance. The present invention achieves this without the need to induce significant damage to the epidermis layer of the skin.

These and other objects are achieved by the present invention which, in one embodiment, provides a method of rejuvenating human skin, the method comprising applying a focused ultrasound beam to a region of human skin to stimulate or irritate a dermis layer in the region of the skin so as to cause a change in the dermis layer of the skin that results in a change in a smoothness of the epidermis layer of the skin.

According to another embodiment of the invention, an apparatus for rejuvenating human skin is provided, the apparatus comprising an ultrasound transducer, coupled to an ultrasound driver, for propagating ultrasound waves into a region of human skin in response to signals from the ultrasound driver, and a control device constructed and arranged to focus the signals provided by the ultrasound driver circuit to control the ultrasound waves provided by the ultrasound driver so as to stimulate or irritate a dermis layer in the region of the skin to cause a cosmetic improvement in an appearance of the skin.

According to another embodiment of the invention, a transducer configuration, capable of applying focused ultrasound energy to a dermis region of human skin is provided. The transducer configuration comprises a transducer and an acoustical waveguide disposed adjacent to an ultrasound emitting surface of the transducer, wherein a thickness of the acoustical waveguide determines a depth focus of the ultrasound energy in the skin.

According to another embodiment of the invention, a method of rejuvenating human skin is provided, the method comprising applying a focused ultrasound beam to a region of human skin to generate a shock wave to mechanically disrupt a dermis layer in the region of the skin so as to cause a change in the dermis layer of the skin that results in a change in a smoothness of an epidermis layer of the skin.

In a further aspect of the invention, the acoustic pulses which are used to treat the skin have pressure amplitudes that are sufficiently high to introduce non-linearity, that is to say, the speed of propagation of the pulses through the target region of dermis will be higher than the normal speed of sound propagation through skin. For example, in skin, the normal speed of sound is approximately 1480 m/sec. However, at high enough amplitudes, skin tissue becomes more elastic and the speed of propagation can increase to as high as about 1500 m/sec. The magnitude of this non-linear behavior varies not only with pulse amplitude, but also with the duration of the pulse. Typically, the non-linear behavior will be exhibited, with acoustic pulses having intensity (within the target region) of about 500 to about 1000 watts/cm^2 and is preferably applied by pulses having durations ranging from about 10 nanoseconds to about 200 microseconds.

One result of this non-linearity is distortion the waveform of the pulses and they travel through the skin, converting waves typically having Gaussian amplitude (pressure) profile to waves that presents a much sharper leading face, essentially a "shock-wave" at the target region below the surface of the skin. In a normal wave propagation mode, there is essentially no net movement of dermal material. However, when acoustic waves exhibit non-linearity, mate-

rial does move, creating a negative pressure, or vacuum effect, in the tissue in the wake of the pulse. This negative pressure can induce the tissue damage of the present invention, tearing tissue structures apart, heating the region and, thereby, triggering the synthesis of new connective tissue.

The invention is particularly useful for reducing the appearance of human skin wrinkles. Embodiments of the present invention can provide a smoother, rejuvenated appearance of the skin, without adversely damaging the epidermis layer of the skin.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, which are incorporated herein by reference and in which like elements have been given like reference characters,

FIG. **1** illustrates one embodiment of an ultrasound generating apparatus according to the invention for reducing skin wrinkles;

FIG. **2** illustrates one embodiment of an ultrasound transducer that may be used in the invention;

FIG. **3** illustrates another embodiment of a transducer that may be used in the invention;

FIG. **4** illustrates another embodiment of a transducer that may be used in the invention;

FIG. **5** illustrates another embodiment of a transducer that may be used in the invention;

FIG. **6** illustrates a control system that may be used to control the apparatus illustrated in FIG. **1**;

FIG. **7** illustrates another embodiment of a transducer that may be used in the invention;

FIG. **8** illustrates a pattern of ultrasound application over a region of skin in accordance with one aspect of the invention; and

FIG. **9** illustrates a pattern of ultrasound application over a region of skin in accordance with another aspect of the invention.

DETAILED DESCRIPTION

FIG. **1** generally illustrates an ultrasound generating apparatus **10** that may be used to apply controlled, localized, focused ultrasound to a region of human skin. The apparatus includes a control circuit **18** coupled to an acoustic wave generator (e.g., an ultrasound transducer) **22** via electrical means **20** which may be a cable or the like. In response to control signals from control circuit **18**, transducer **22** generates ultrasound waves **21**. Transducer **22** may have one or more elements, such as piezoelectric elements, that actually produce the ultrasound or similar acoustic waves. A focusing element **24**, an acoustically-transmitting waveguide **26**, and an acoustical coupling medium **28** (either alone or in combination) may also be provided to direct and focus the ultrasound waves produced by transducer **22**. Acoustical coupling medium **28** may be a biocompatible hydrogel.

Apparatus **10** is used to direct the ultrasound waves **21** into skin **12**. The ultrasound waves are focused using focusing element **24** so that the focused ultrasound waves create a region of stimulation and/or irritation **30** in the dermis layer **16** of skin **12**. Focusing ultrasound waves **21** within region **30** allows localized enhancement of the fluence of the ultrasound beam directed into the skin in region **30**. This allows a significant part of the energy in ultrasound waves **21** to be substantially absorbed in region **30**. This results in stimulation and/or irritation of region **30**. Since the region **30** is principally contained in dermis layer **16**, there should be little, if any, significant adverse damage to the epidermis layer **14**.

The term "ultrasound" as used in this disclosure is intended to encompass both conventional "ultrasound" as typically used to describe high-frequency acoustic waves up to about 100 megahertz and "hypersound" as typically used to describe very high frequency acoustic waves greater than about 100 megahertz. In general, "ultrasound" is used within this disclosure to describe acoustic waves capable of inducing controlled hyperthermia or cavitation in skin tissue, or pulsed waves having an amplitude large enough to induce shock waves in the skin tissue. Hyperthermia, as used in this disclosure, is a condition in which an elevated temperature is induced in a region of the body for therapeutic purposes.

As noted, a feature of the invention lies in providing a focused ultrasound beam that irritates and/or stimulates the dermis layer of the skin without significant or detrimental irritation of the epidermis layer. In FIG. **1**, focusing of the ultrasound beam was provided by focusing element **24** which may be a type of lens.

The apparatus illustrated in FIG. **1** is similar to the apparatus described in U.S. Pat. No. 5,230,334, issued to the same inventor. The '334 patent describes a method and apparatus for generating localized hyperthermia in human tissue, particularly in the collagen fibers of the cornea. This previous work has been improved upon by the present invention. One difference lies in the biological mechanism by which the present invention is hypothesized to work. In the '334 patent, the application of relatively high power, controlled hyperthermia, causes the collagen fibers in the cornea to mechanically shrink during the duration of, or immediately after, application of the ultrasound energy to the cornea. This is to be contrasted with the hypothesized mechanism of the present invention in which relatively low power ultrasound is used to gently stimulate and/or irritate the dermis to induce a biological response that results in synthesis or production of new connective tissue over a period of time that extends beyond the time of application of the ultrasound energy. It is envisaged that treatment by the present invention may require multiple treatments extending over a relatively long period of time, such as days, weeks, or months, in order to stimulate the body to produce new connective tissue in the dermis layer and would not cause significant damage to the epidermis. Use of the power levels contemplated in the '334 patent in this manner would cause severe damage to the epidermis.

FIG. **2** illustrates another configuration of transducer **22** for providing a focused ultrasound beam. In FIG. **2**, transducer **22** has a concave or cylindrical surface **40** that extends along dimension **42**. A number of elongated transducer elements, such as piezoelectric elements **44** are disposed along a surface **46** of region **40**. One skilled in the art will appreciate that a single curved transducer or multiple transducer elements could be used in transducer **22**. Elements **44** extend longitudinally along the direction of dimension **42**. Since elements **44** are disposed along the concave surface, they will transmit the ultrasound beams that they respectively generate towards a focal point **48** that lies at the intersection of the various radii **50** that extend from transducer elements **44** to focal point **48**. Thus, by adjusting the radius of curvature of surface **46**, the location of focal point **48** can be changed. One skilled in the art will appreciate that focal point **48** extends longitudinally along the direction of dimension **42** to create a scanline **43**.

FIG. **3** illustrates another transducer configuration that can be used in accordance with the present invention. In

FIG. 3, transducer 22 is fitted with an acoustical waveguide 54 that covers a surface 56 of the transducer. Acoustical waveguide 54 is analogous to acoustical waveguide 26 illustrated in FIG. 1. An acoustical coupling medium, preferably of a material having the same or similar transmissive properties as acoustical waveguide 54 fills the entire cavity 52. Alternatively, acoustical waveguide 54 can be a single piece that additionally fills cavity 52. The transducer illustrated in FIG. 3 performs in the same manner as transducer 22 illustrated in FIG. 2 however, the addition of acoustical waveguide 54 can make the transducer easier to scan across flat skin surfaces. In addition, acoustical waveguide 54, since it acts to direct the ultrasound waves along the direction of radii 50, can reduce the size and bulk of transducer 22. That is, the addition of acoustical waveguide 54 may allow the radius of curvature of surface 46 to be larger than what would otherwise be required, without waveguide 54, for a given location of focal point 48. Thus, this particular configuration of ultrasound transducer 22 may be easier to manufacture than one having its radius of curvature determined only by the location of focal point 48. This configuration is also useful when higher ultrasound beam intensities are being used because it can prevent overheating of the transducer since the transducer can be made physically larger to better dissipate heat.

In the present invention, the depth of focus of scanline 43 is very close to the surface of the skin, therefore, acoustical waveguide 54 can be used to determine the depth of focus. Acoustical waveguide 54 can be of differing thickness where each different thickness provides a different depth of focus. Use of acoustical waveguides of differing thickness provides a convenient means for changing the depth of focus which can be advantageous in the case where treatment is carried out in, for example, a doctor's office.

FIG. 4 illustrates another transducer configuration that can be used in accordance with the present invention. In FIG. 4, transducer 22 has a flat or planar configuration and transducer elements 44 are disposed in an essentially planar fashion. A lens 24 having a focusing portion 25 is disposed along the lower surface 56 of the transducer. Focusing section 25, which is cylindrical and extends along the direction 42, acts to focus the ultrasound wave generated by transducer elements 44 along the direction of lines 50 so that the ultrasound waves produced by transducer elements 44 are focused at focal point 48.

FIG. 5 illustrates another transducer configuration that can be used in accordance with the present invention. In FIG. 5, transducer 22 is fitted with an acoustical waveguide 54 disposed at the lower surface 58 of lens 24. Acoustical waveguide 54, in the same manner described in connection with FIG. 3, allows the radius of curvature of focusing section 25 of lens 24 to have a larger radius of curvature than would otherwise be required for a given location of focal point 48. Thus, this particular configuration of ultrasound transducer 22 may be easier to manufacture.

The systems illustrated in FIGS. 1, 2, 3, 4, and 5 should strongly focus the ultrasound beam with a numerical aperture in the range of approximately 0.1 to approximately 0.95. As illustrated in the figures, the lens preferably has a cylindrical geometry.

One skilled in the art will also appreciate that a biocompatible hydrogel may be placed between the skin surface and the lens 24 (in the case of FIG. 4) and acoustical wave guide 54 (in the case of FIG. 5).

One skilled in the art will appreciate that although particular transducer configurations have been illustrated in FIGS. 1–5, a variety of other transducer configurations can be used in the present invention. In addition, a phased array ultrasound transducer could be used. A phased array may be advantageous in that it can be used to focus the ultrasound beam generated by each respective transducer element at a desired focal point depth and location. In addition to focusing the ultrasound beam, the phased array can be used to scan the ultrasound beam over the area of skin to be treated.

FIG. 6 illustrates a control system that may be used in the present invention to control the amount of energy provided to region 30 of dermis layer 16. The control system 100 includes a controller 102. Controller 102 may include a computer and associated peripherals such as memory and mass storage devices. An operator interface 104, which may include at least a keyboard and display device, allows the user to set various parameters such as the focal point depth, the magnitude of the ultrasound beam to be applied, the duration that the ultrasound beam will be applied, and so on. Control signals from controller 102 are sent to a driver 106. Driver 106 contains means, such as circuitry, such as needed to cause the transducer element or elements of transducer 22 to generate ultrasonic waves.

Control system 100 thereafter includes five different feedback systems that may be used to control the dose of ultrasound energy applied to a patient's skin. One skilled in the art will appreciate that the five feedback systems may be used individually or in any combination.

The first feedback system includes a receiver 110 and a signal analyzer 112. Receiver 110 and signal analyzer 112 may be used to measure the magnitude of the ultrasound energy being applied to the patient's skin and to provide a feedback signal to controller 102 to automatically, or allow the operator to manually adjust the magnitude of the ultrasound beam being delivered by transducer 22.

The second feedback system includes a temperature sensor 114 that may be used to measure the temperature of the skin in the region where the ultrasound energy is being applied. Using temperature sensing as a feedback mechanism can be effective because the surface of the skin where temperature sensor 114 would be located is in close proximity to the region of the skin being heated by ultrasound energy. The sensed temperature reading can then be used by controller 102 to automatically, or manually, under control of the operator, to control the magnitude of ultrasound energy being delivered to the patient's skin by transducer 22.

The third feedback system includes a second ultrasound transducer 116 and transceiver 118. Transceiver 118 and transducer 116 can be used to provide a low level ultrasound signal that can be used for diagnostic and feedback purposes to controller 102. Transceiver 118 and transducer 116 can also be used as an echolocating system for target location. That is, the low power ultrasound signals can be used to locate microorgans, such as hair follicles, in the skin to aid in treatment.

Furthermore, if driver 106 is replaced with a transceiver or if an additional receiver is provided and connected to transducer 22 and controller 102 then the echolocating function can be performed using one transducer. That is the transducer 22 may be placed on the patient's skin and, under control of controller 102, low power ultrasound waves can be used for target location and placement. Once a location for treatment has been established, controller 102 can be switched to a treatment mode and a higher power ultrasound wave may then be applied using transducer 22 to treat the skin.

More generally, the low power ultrasound may be used to locate a condition below the epidermis that causes an

irregularity in the smoothness of the epidermis. Higher power ultrasound can then be used to treat the area.

Furthermore, the low power ultrasound signal can also be used to automatically determine the depth of focus for the ultrasound energy. For example, the low power or diagnostic ultrasound signal can be used to locate the depth of the interface between the dermis and the epidermis in the area to be treated. The depth of focus for the high power or therapeutic ultrasound can then be set based on this measurement to ensure that the ultrasound energy is focused in the dermis layer.

The fourth feedback system includes an electrical conductivity sensor **120** that may be used to measure the electrical conductivity of the patient's skin in the region where the ultrasound energy is being applied. The degree of electrical conductivity sensed by sensor **120** can then be used by controller **102** to automatically, or manually, under control of the operator, control the magnitude of ultrasound energy being delivered to the patient's skin by transducer **108**.

The fifth feedback system includes a broadband microphone **122** connected to controller **102**. When cavitation is used as a mechanism to provide dermal irritation, microphone **122** can be placed on or near the skin in the region being treated. The collapse of a bubble created by application of ultrasound in the dermis creates a characteristic audible sound that is detected by microphone **122**. The signal provided by microphone **122** can then be used by controller **102** with appropriate signal processing to control the ultrasound energy provided by transducer **22**. The user can also listen to the signal provided by microphone **122** and manually control the ultrasound energy.

Controller **102** should be programmed so that transducer **22** delivers a spatially uniform ultrasound dosage in the area of the skin that is being treated to ensure uniform stimulation of the dermis layer. The method of the invention appears to be most effective when there is, on average, a homogeneous deposition of energy in the region of the skin that is being treated.

Referring to FIG. **7** transducer **22** is illustrated as being scanned along a direction defined by double-headed arrow **45**. While transducer **22** is being scanned along the direction of arrow **45**, it is delivering an ultrasound beam focused at a focal point or depth **48** in the dermis layer of the skin. Focal point **48** extends longitudinally along the direction of dimension **42** to create a scanline **43**. Controller **102** therefore needs to be programmed to deliver a uniform level of energy in two dimensions; one along the direction or dimension **42** and one in a direction of scanning along line or dimension **45**.

The energy delivered by transducer **22** into the skin may be delivered in a continuous manner or in discrete increments. One skilled in the art will appreciate that the ultrasound energy may be continuous in one dimension for example, dimension **42** and discrete in another dimension, for example dimension **45** or vice versa. One skilled in the art will appreciate that the ultrasound energy may be delivered continuously in both dimensions or discretely in both dimensions.

If the ultrasound energy is delivered discretely in both dimensions **42** and **45**, then a pattern of ultrasound energy application such as illustrated in FIG. **8** results where each point **47** represents a location where ultrasound energy has been applied. If the ultrasound energy is applied in a manner that is continuous in both dimensions **42** and **45**, then the area in between points **47** would also have ultrasound energy applied thereto.

If the ultrasound energy is delivered discretely in dimension **45** and continuously in dimension **42**, then a pattern of ultrasound energy application such as illustrated in FIG. **9** results where regions **49** represent regions where ultrasound energy has been applied.

In the case of continuous ultrasound application, both the speed of scanning along direction **45** and the power being applied must be controlled simultaneously. In the same manner, if discrete application of ultrasound energy is being used, then the distance between points **47** along the direction of arrow **45**, the speed with which transducer **22** is moved along the direction of arrow **45**, and the timing of individual energy deposition must be controlled to provide homogeneous exposure.

As illustrated in FIGS. **6** and **7** an encoder **124** may be provided. Encoder **124** may be, for example, a wheel that rolls along the skin as the transducer is scanned across the skin. An electrical signal which may be analog or digital in nature, is then provided to controller **102**. Controller **102** uses the signal from encoder **124** to determine the speed with which transducer **22** is being scanned across the skin surface and the distance being traveled. With this information, controller **102** can be programmed to adjust the ultrasound pulse frequency and intensity of the ultrasound energy in relation to the scanning speed and distance traveled to achieve, on average, spatially uniform ultrasound dosage if discrete ultrasound pulses are being used. In the same manner, if continuous power is being used, then controller **102** will adjust the ultrasound beam energy in relation to scanning speed to achieve a homogeneous application of ultrasound energy in the target area.

In another embodiment, an acoustically transparent plate may be placed on the skin over the area to be treated and then transducer **22** and encoder **124** are then scanned across the acoustically transparent plate. Scanning the transducer across the plate can also provide a way of delimiting the area to be treated to avoid over-treating or under-treating the area of the skin.

To use the method and apparatus of the invention to reduce or eliminate human skin wrinkles, a physician or technician ("the user") sets a desired depth of the focal point for the ultrasound beam so that the ultrasonic energy is substantially concentrated in the dermis layer of the skin. This depth is typically in the range of five microns to five millimeters. The magnitude of the ultrasound energy to be deposited in the dermis layer in also determined. The duration of treatment and the volume of the dermis layer to be stimulated and/or irritated determine the power level necessary.

The frequency of the ultrasound beam is also chosen. The ultrasound wave frequency should be within the range between approximately 1 megahertz and 500 megahertz. Preferably, the ultrasound beam frequency is relatively low frequency ultrasound between the range of approximately 10 and 80 megahertz. The ultrasound beam frequency chosen is based upon a consideration of the depth of penetration of a given ultrasound frequency wave into the skin and the power required to cause an appropriate stimulation and or irritation of the dermis region of interest.

Obviously, the above-described steps may be performed in any order.

Once these parameters have been set, the ultrasound transducer is then scanned over the wrinkle area of the skin. Typically, an area much larger than or extending significantly beyond the area occupied by the wrinkle is subjected to the ultrasound beam. Preferably, to be effective, the area

of the skin that is subjected to treatment is on the order of ten times larger than the area of the wrinkle itself.

Although the biological mechanism is not completely understood, it appears that hyperthermia and/or cavitation, either alone or in combination, appear to cause a biological response. It appears that denaturation by hyperthermia of at least some of the intracellular proteins, intercellular proteins, and/or enzymes induces a biological or healing response in the body. The biological response results in the synthesis of new connective tissue by fibroblast cells in the dermis in addition to the preexisting connective tissue. The new connective tissue fills out the skin. It is the process of adding new connective tissue to the dermis layer that causes reduction in the appearance of skin wrinkles and improved shape, smoothness, and appearance of the skin.

One mechanism by which the biological response may be stimulated is through hyperthermia. The amount of energy deposited using hyperthermia is typically that required to raise the temperature of the dermis layer to somewhere is the range of 47° C. to 75° C. Preferably, the temperature of the dermis layer that is being treated is increased to between approximately 55° C. and approximately 65° C.

These ranges are selected so as to denature a relatively small fraction of the proteins in the dermis. At a temperature of approximately 47° C., it takes several tens of seconds to denature a small fraction of the proteins in the dermis. By contrast, at a temperature of 73° C., the same small fraction of the proteins in the dermis are denatured in several tens of microseconds. One skilled in the art will appreciate that there is a trade off between exposure time and the amount of energy being applied. The higher the level of energy to be applied, the lower the required exposure time and vice verse. Elevating the dermis layer to a temperature in approximately the range from 55° C. to 65° C. appears to provide a workable compromise between the length of time for the treatment and the amount of energy to be imparted to the skin.

Another mechanism by which a biological response may be induced is cavitation. Preferably, when using cavitation alone or in combination with hyperthermia, enough energy needs to be applied to the dermis to generate, in the dermis, a cavitational bubble. When the bubble collapses, a shock wave results that mechanically, in as localized area, tears apart tissue in the dermis causing dermal inflammation or irritation and a resultant biological response. The biological response results in the synthesis of new connective tissue.

Another mechanism by which a biological response may be induced in through the use of pulsed acoustic waves. Pulsed acoustic waves having sufficient amplitude may be used to create a negative pressure wave at the focal point so as to induce a shock wave type response in the dermis. As with the collapse of the cavitational bubble, the shock wave mechanically, in a localized area, tears apart tissue in the dermis causing a dermal irritation and a resultant biological response. The biological response results in the synthesis of new connective tissue.

It will be appreciated that the magnitude of energy deposited in the skin as a function of the frequency of the ultrasound wave, the time the ultrasound wave is applied, the area of the skin that is treated, thermal diffusion of the heat in the skin, and the impedance of the skin to ultrasound energy may be varied to provide the desired biological response. The present invention typically uses dosages that are significantly lower than conventional hyperthermia therapies. For example, at the surface of the epidermis, the intensity of the ultrasonic waves may be in the range of approximately 100 to 500 watts/cm^2. At the focal point in the dermis layer, under some conditions, the intensity of the ultrasonic waves may be in the range of approximately 500 to 1500 watts/cm^2.

It should be noted that the method of the present invention does not, following application of ultrasound energy, immediately cause skin wrinkles to be reduced or to disappear. The treatments typically need to be repeated over a long period of time (such as days or months) so that the dermis layer is gently stimulated or irritated to produce the biological response while at the same time avoiding catastrophic damage to the epidermis layer. This has a number of advantages over conventional methods. First, the epidermis is not damaged or is only minimally damaged or effected. Second, the dermis layer is not exposed so the chance of opportunistic infection is reduced. Third, due to the relatively low power levels used and the fact that the epidermis is not catastrophically damaged, the discomfort and pain to the patient compared to conventional methods is considerably reduced.

As noted, the method of the invention using hyperthermia aims to denature a relatively small fraction of the proteins in the dermis, typically less than twenty percent of the proteins. These proteins may be intracellular, extracellular, or also enzymes. Preferably less than ten percent of the proteins in the dermis are denatured and, to be certain that there is much less damage to the cells of the epidermis, no more than approximately five percent of the proteins in the dermis should be denatured.

To further prevent elevation of the temperature or irritation of the epidermis layer of the skin, a cooling device or method may be used. A sapphire tip may be disposed on the ultrasound transducer. Alternatively, water cooling may be used before, during, or after treatment. One skilled in the art will appreciate that there are numerous cooling devices or methods that could be used in conjunction with the invention.

Heating or cooling of the skin can also be used to bring the temperature of the skin to a known state prior to treatment so as to control the dosage of applied ultrasound. This can be significant since denaturation of proteins is dependent on the absolute temperature of the skin and not the relative temperature increase with respect to the starting skin temperature. Heating or cooling of the skin can also be used to take into account patient-to-patient variability such as differing body temperatures to bring all patients to the same state before treatment.

A marker may also be used to delimit treatment areas. The marker may be any kind of suitable marker. For example, a fluorescent gel may be deposited on the skin as the transducer is scanned across the skin. Ink, paint, or disinfectant may also be used. The marker may be visible or may be invisible except when exposed with a suitable light source. A marker allows the user to guide the transducer to produce a spatially uniform ultrasound dosage to ensure uniform stimulation of the dermis and avoid over-treating areas of the skin while under-treating others.

The invention may also reduce other types of defects in skin appearance, such as acne scars and burns, and rejuvenate or refresh skin appearance. This is, as the new connective synthesized in response to the stimulation or irritation of the dermis begins to fill out the dermis, these types of skin defects may become less visible and the skin takes on smoother, refreshed or rejuvenated look.

Having thus described at least one illustrative embodiment of the invention, various alterations, modifications, and

improvements will readily occur to those skilled in the art. For example, various alternative acoustic pulse or "shock-wave" generators can be employed in lieu of the above described ultrasound transducers. Such alternative energy generators include piezoelectric, electric spark and laser-triggered pulse forming devices operating on rapid state changes of liquid media or on thermoelastic expansion. The pulse generated by these devices can exhibit broad frequency domains. Accordingly, the foregoing description is by way of example only and is not intended as limiting. The invention is limited only as defined in the following claims and the equivalents thereto.

What is claimed is:

1. A method of rejuvenating skin, the method comprising applying an acoustic pulse to a dermis layer below a surface of a region of skin with sufficient intensity and duration, and inducing a shock wave response in the dermis layer and consequent formation of new connective tissue to cause a change in the dermis layer of the skin that results in greater smoothness at the surface of the skin.

2. The method of claim 1, wherein a step of inducing formation of new connective tissue further comprises elevating the temperature of the dermis layer.

3. The method of claim 1, wherein the step of applying an acoustic pulse further includes applying a focused ultrasound beam for a time sufficient to cause proteins in the dermis layer to denature.

4. The method of claim 1, wherein the step of applying an acoustic pulse further comprises applying a power level in the range of approximately 500 W/cm^2 to 1500 W/cm^2 within a target region of the dermis.

5. The method of claim 1, wherein the step of applying an acoustic pulse to a dermis layer further comprises focusing a ultrasound beam at a depth below the epidermis in a range between approximately 5 microns and 5 millimeters.

6. The method of claim 1, wherein the step of inducing formation of new connective tissue further comprises inducing cavitation in the dermis layer.

7. The method of claim 1, wherein a step of inducing formation of new connective tissue further comprises irritating the dermis layer without adversely damaging the epidermis layer.

8. The method of claim 1, wherein the region of skin includes a wrinkle and the method further comprises the step of scanning the focused ultrasound beam over an area occupied by the wrinkle.

9. The method of claim 8, wherein the step of scanning further comprises scanning the focused ultrasound beam over an area of the skin that is approximately ten times larger than an area of the wrinkle.

10. The method of claim 1, further comprising a step of cooling the region of skin at least one of before, during, or after the step of applying the acoustic pulse.

11. An apparatus for rejuvenating skin, the apparatus comprising:

an acoustic wave generator for transmitting acoustic waves into a dermis region of skin in response to signals from a driver; and

a control device constructed and arranged to control the generator to induce shock-waves in the dermis layer and the formation of new connective tissue.

12. The apparatus of claim 11, wherein the control device controls the ultrasound waves to elevate the temperature to a range and for a time sufficient to cause proteins in the dermis layer to denature.

13. The apparatus of claim 11, wherein the apparatus further comprises an acoustic lens to focus the acoustic energy at a depth below the epidermis in a range between approximately 5 micrometers and 5 millimeters.

14. The apparatus of claim 11, wherein the control device controls the acoustic waves to have at least one frequency between approximately ten megahertz and one hundred megahertz.

15. The apparatus of claim 11, wherein the apparatus further comprising a temperature sensor coupled to and providing a temperature signal to the control device.

16. The apparatus of claim 11, further comprising an acoustic receiver, coupled to at least one of the acoustic wave generator and the control device.

17. The apparatus of claim 11, further comprising a cooling device that cools the temperature of the epidermis layer.

18. The apparatus of claim 11, wherein the control device controls the acoustic waves to apply a power level in the range of approximately 500 W/cm^2 to 1500 W/cm^2 within a target region of the dermis.

19. The apparatus of claim 11, wherein the control device controls the acoustic waves to durations ranging from about 10 nanoseconds to about 200 microseconds.

20. An apparatus for rejuvenating skin, the apparatus comprising:

an acoustic wave generator for delivering acoustic wave energy into a dermis layer of of skin; and

a controller for driving the acoustic wave generator to deliver pulsed acoustic wave energy at a sufficient amplitude and frequency to induce a shock wave type response in the dermis layer.

21. The apparatus of claim 20, wherein the controller includes circuitry to drive the wave generator to deliver pulsed acoustic wave energy having at least one frequency between approximately ten megahertz and one hundred megahertz to induce a shock wave type response in the dermis layer.

22. An apparatus for rejuvenating skin, the apparatus comprising:

an acoustic wave generator for delivering acoustic wave energy into a dermis layer of a region of skin; and

a controller for driving the acoustic wave generator to deliver pulsed acoustic wave energy, the pulses ranging from about 10 nanoseconds to about 200 microseconds in duration, each pulse delivering energy in the range of about 500 W/cm^2 to about 1500 W/cm^2 at a target site in the dermis layer to induce a shock wave type response in the dermis layer.

23. An apparatus for rejuvenating skin, the apparatus comprising:

an acoustic wave generator for delivering acoustic wave energy into a dermis layer of skin;

a controller for driving the acoustic wave generator to deliver pulsed acoustic wave energy at a sufficient amplitude and frequency to induce a shock wave type response in the dermis layer; and

a linear focusing element for focusing the acoustic energy into a line such that an elongated region of the dermis layer is exposed to the acoustic wave energy.

24. The apparatus of claim 23 wherein the acoustic wave generator comprises at least one ultrasound transducer and the focusing element comprises an elongated surface of the transducer.

25. The apparatus of claim 23 wherein the acoustic wave generator comprises at least on ultrasound transducer and the focusing element comprises at least one cylindrical lens.

26. The apparatus of claim 23, wherein the focusing element focuses the ultrasound energy in a region at a depth

below the epidermis in a range between approximately 5 microns and 5 millimeters.

27. An apparatus for rejuvenating skin, the apparatus comprising:

an acoustic wave generator for delivering acoustic wave energy into a dermis layer of skin;

a controller for driving the acoustic wave generator to deliver pulsed acoustic wave energy at a sufficient amplitude and frequency to induce a shock wave type response in the dermis layer; and

a focusing element for focusing the acoustic energy into the dermis layer, the focusing element having a numerical aperture ranging from about 0.1 to about 0.95.

28. The apparatus of claim 27, wherein the controller drives the acoustic wave generator to deliver pulsed acoustic wave energy at sufficient energy to elevate the temperature of a region within the dermis layer, preferably, to a range between approximately 47° C. and 75° C.

29. The apparatus of claim 28, wherein the controller controls the ultrasound waves to elevate a temperature of the dermis layer, preferably, to a range between approximately 55° C. and 65° C.

30. An apparatus for rejuvenating skin, the apparatus comprising:

an acoustic wave generator for delivering acoustic wave energy into a dermis layer of skin;

a linear focusing element for focusing the acoustic energy into a line such that an elongated region of the dermis layer is exposed to the acoustic wave energy to induce a shock wave type response in the dermis layer; and

a scanner for scanning the line through an area within the dermis layer.

31. An apparatus for rejuvenating skin, the apparatus comprising:

an acoustic wave generator for delivering acoustic wave energy into a dermis layer of of skin; and

a controller for driving the acoustic wave generator to deliver pulsed acoustic wave energy at sufficient amplitude to induce a shock wave response in the dermis layer; and

at least one feedback sensor for sensing the effect of the delivered energy and providing a signal to the controller.

32. The apparatus of claim 31, wherein the feedback sensor comprises a temperature sensor coupled to and providing a temperature signal to the controller.

33. The apparatus of claim 31, wherein the feedback sensor comprises an ultrasound receiver, coupled to the ultrasound transducer, and a signal analyzer that processes a signal received by the ultrasound receiver to provide a feedback signal to the controller.

34. The apparatus of claim 31, wherein the feedback sensor comprises an electrical conductivity sensor coupled to and providing to the control device a measure of electrical conductivity in the area of skin where ultrasound energy is being applied.

35. The apparatus of claim 31, wherein the feedback sensor comprises an audio sensor coupled to and providing to the control device an audio signal of the area of skin where ultrasound energy is being applied.

36. The apparatus of claim 35, wherein the audio sensor is a broadband microphone.

37. The apparatus of claim 31, further comprising a cooling device that cools the epidermis layer.

38. An apparatus for rejuvenating skin, the apparatus comprising:

a transducer for delivering acoustic wave energy into a dermis layer of skin; and

an acoustical waveguide disposed at a surface of the transducer, the waveguide having a thickness that defines a depth focus of the ultrasound energy in the skin; wherein the waveguide is further arranged to apply ultrasound shock waves along a longitudinally extended area.

39. The apparatus of claim 38, wherein the waveguide further comprises a cylindrical acoustic lens for applying the ultrasound waves along the longitudinally extended area.

40. The apparatus of claim 38, wherein the waveguide further comprises an acoustically transparent plate for disposition over the area of skin to be treated so as to delimit the area to be treated.

41. The apparatus of claim 38, wherein the waveguide further comprises an acoustic focusing lens has a numerical aperture ranging from about 0.1 to about 0.95.

* * * * *

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 872 262 A2

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
21.10.1998 Bulletin 1998/43

(51) Int. Cl.[6]: **A61N 7/02**

(21) Application number: **98106818.2**

(22) Date of filing: **15.04.1998**

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: **18.04.1997 SE 9701449**

(71) Applicant:
Scandimed International AB
275 37 Sjöbo (SE)

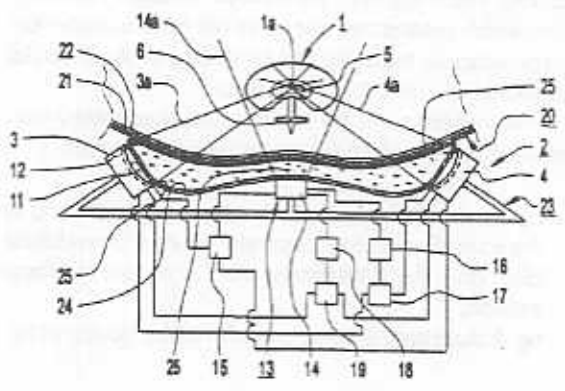
(72) Inventors:
- **Lidgren, Lars**
  227 31 Lund (SE)
- **Strömqvist, Björn**
  237 31 Bjärred (SE)
- **Severson, Johan**
  224 58 Lund (SE)

(74) Representative:
Wagner, Karl Heinz
H. Wagner & Co. AB
Norra Vallgatan 72
211 22 Malmö (SE)

(54) Device for non-invasive treatment of biological tissue

(57) The present invention relates to a device for non-invasive treatment of biological tissue, whereby the treatment aim at changing or degenerating said tissue. This device has a treatment transducer (2) comprising at least one ultrasonic transducer (3 and/or 4) which is provided to treat intervertebral discs (1), preferably nucleus pulposus (1a), by means of ultrasound, whereby the ultrasonic field of the ultrasonic transducer (3 and/or 4) is focused in said intervertebral disc (1), preferably in nucleus pulposus (1a), for heating the tissue therein, to such temperatures that the tissue in the focal area (5) degenerates, whereby the pressure in the intervertebral disc (1) and thus, the pressure against the spinal cord (6) is reduced.

Fig. 1



EP 0 872 262 A2

Description

The present invention relates to a device for non-invasive treatment of biological tissue, whereby the treatment aim at changing or degenerating said tissue.

The lifetime prevalence of sciatica is 40 percent and 1-2 percent of the population will develop nerve compression by a lumbar disc herniation requiring invasive (surgical) treatment, usually during the fourth and fifth decades of life. Surgical removal of discal hernia, discectomy, has been performed for almost seven decades. The diagnostic procedures going from myelography using oil to nonionic contrastmedia over to computerized tomography (CT) and magnetic resonance imaging (MRI) has led to a rapid increase of the number of spinal operations based on diversity of surgical procedures.

There are four necessary prerequisites for intervention of disc herniation: a/ functionally incapacitating pain in the leg extending below the knee with a nerve root distribution, b/ nerve root tension signs with or without neurological abnormalities, c/ failure of clinical improvement after four to eight weeks, d/ diagnostic confirmation (e.g. through imaging study).

The introduction of non-surgical or minimal invasive surgical procedures started 1964 with chymopapain and chemonucleolysis which brought about the era of percutaneous treatment for herniated discs. The clinical success of chymopapain with good results in 60-75 percent led to an extensive use. Unfortunately, it had an anaplylaxis rate estimated to be about 1 percent. The enzyme polymerizes the long chains of proteoglycans in the nucleus pulposus with subsequent loss or water binding capacity. This causes reduction in the volume and pressure of the nucleus and the herniated fragment, eventually explaining the immediate relief of sciatica in patients following chemanucleolysis. Most authors agree that relief of leg pain after chymopapain is less frequent than after surgery. Several new methods using percutaneous techniques have evolved since 1975, using endoscopic equipment and recently also non-endoscopic technique with an automated percutaneous suction of tissue by means of a probe. Recently, laser (electromagnetic) radiation created by external stimulation of a laser medium, has been used. For directing the laser radiation to the treatment area however, a probe is required, i.e. the method is invasive.

All these methods are to a certain extent invasive (require surgical operations) and problems such as disc infection and nerve root injury are encountered although less frequently than after open surgery.

The intervertebral disc is comparable to other non-vascularized biological tissue. It has a central nucleus pulposus with a gelatinous character and a surrounding stiffer anulus. The matrix in the disc includes several proteins with different rates of turn over and energy demand.

There is today no non-invasive treatment that will affect the disc in such a manner that it will reduce its volume and pressure in the nucleus and thereby possibly diminish a discal hernia.

Attempts to achieve tissue degeneration with high intensity focused ultrasound (HIFU) have been going on for several years in cancer research projects (Bush 1993, Billard 1990, Lele 1980, Linke 1973, Sibille 1993). The advantage of ultrasound as a generator of energy, compared to e.g. electromagnetic fields, is that ultrasound is a non-invasive method to generate tissue heating at depths. Focusing of the ultrasound and placing the focus inside the tissue to be treated, makes the heating effect to develop at the desired location instead of at the skin and the tissue in between (Lele 1980). If the transducer surface is spherical, the transducer has a fixed focus (Lele 1980). It is also possible to achieve a flexible focus by means of phased array (Diederich 1991, Ebbini 1988, Ebbini 1991 and Holmer 198?).

Prior art also includes a number of patent specifications relating to methods and devices wherein ultrasound is utilized for various therapeutic purposes without any type of surgical operations on the patient. One such patent specification is US-A-5 435 311 relating to an "ultrasound therapeutic system" for treatment of e.g. malignant tumours or various types of calculi such as gallstone, kidney stone, etc.. The device of US-A-4 787 394 relating to an "ultrasound therapy apparatus", has a similar purpose.

Other devices and methods utilizing ultrasound for a corresponding therapeutic purpose, are described in e.g. US-A-5 327 884 and US-A-5 501 655.

Similar tissue degeneration as with ultrasound can also be made with other methods, such as percutaneous laser discectomy and percutaneous radio-frequency coagulation by means of cauterizing instruments (Buchalt 1992, Troussier 1995), but these methods are invasive.

The object of the present invention has been to provide a device for non-invasive treatment of back problems. This is arrived at according to the invention by providing the initially defined device with the characterizing features of claim 1.

By providing the device with said characterizing features, it is possible to treat intervertebral discs, preferably nucleus pulposus, in a lenient manner, i.e. without degenerating tissue outside the intervertebral disc and this treatment can be carried through non-invasively, which means that one does not have to insert foreign objects into the body and obviates thereby the risks and additional costs this might incur.

The invention will be further described below with reference to the accompanying drawings, in which

fig. 1 schematically illustrates a device according to the invention during treatment of an intervertebral disc, whereby a treatment table is shown in cross-section;

fig. 2 illustrates an enlarged part of the device of fig.

1;

fig. 3 schematically illustrates a treatment transducer forming part of the device of fig. 1 and its ultrasonic field during treatment of the intervertebral disc;

fig. 4 is a flow chart according to which the treatment of the intervertebral disc is carried through by means of the device according to the invention; and

fig. 5 is a picture of an intervertebral disc treated with the device according to the invention.

The device illustrated in the drawings is intended for treatment of biological tissues in the form of intervertebral discs 1, preferably nucleus pulposus 1a. For this purpose, the device comprises a treatment transducer 2 which includes two ultrasonic transducers 3 and 4 (so called therapeutic transducers). These are arranged to each transmit an ultrasonic field 3a and 4a respectively, such that these meet to define a focal area 5. During treatment, said focal area 5 is located in the intervertebral disc 1, preferably nucleus pulposus 1a, to be treated for heating the tissue therein to such temperature that the tissue in the focal area 5 degenerates, whereby the pressure in the intervertebral disc 1 and thus, the pressure against the spinal cord 6, is reduced.

The ultrasonic transducers 3, 4 are provided to transmit ultrasonic fields 3a, 4a which to not heat biological tissue outside the focal area such that it degenerates. By using at least two ultrasonic transducers 3, 4, the ultrasound effect is distributed over larger areas and therefore, a lower power per transducer can be used. This results in that eventual heat increases in the skin are minimized for the power to be put in the intervertebral disc 1.

The power and frequency of the ultrasonic fields 3a, 4a, the temperature of the tissue in the focal area 5 and the transmitting time of the ultrasonic fields 3a, 4a may vary depending on various factors, but the frequency should lie within the range of 0,5 - 2,5 MHz, the temperature of the tissue in the focal area within the range of 45-80°C and the total transmitting time of the ultrasonic fields 3a, 4a within the interval of 5-60 minutes.

The ultrasonic transducers 3, 4 can be arranged to transmit ultrasonic fields 3a, 4a, the focal area 5 of which is adaptable relative to the space M between the end plates 7, 8 surrounded by the vertebrae 9, 10 and which surround the intervertebral disc 1, such that said focal area 5 can lie between the end plates 7, 8 without heating thereof to tissue-degenerating temperatures.

A focal area 5 with such adapted extension can be obtained by providing the ultrasonic transducers 3 and 4 respectively, with means 11, preferably in the form of transducer elements with concave spherical transducer surface. Hereby, a larger or better focussing is achieved and the focal area 5 can be given a substantially planar extension, as is shown in fig. 3.

The ultrasonic transducers 3, 4 may also include means 12 for, if required, displacing the focal area 5, adapted preferably as mentioned to the space M between the end plates 7, 8, to the intervertebral disc 1, preferably nucleus pulposus 1a. These means 12 can be transducer elements of the phased array type.

For being able to locate to focal area 5 in the intervertebral disc 1, preferably nucleus pulposus 1a, it may sometimes - depending on the relative positions of the ultrasonic transducers 3, 4 and the intervertebral disc 1 - be advantageous or necessary to shrink or reduce the extention of one or both the ultrasonic fields 3a, 4a for avoiding heating of tissue outside the intervertebral disc 1 which may not be heated to tissue-degenerating temperatures. This can be achieved while the ultrasonic transducers 3, 4 have a plurality of means 12, preferably said transducers of phased array type, which momentarily can be deactivated or put out of operation for reducing the extension of the ultrasonic field 3a and/or 4a.

The ultrasonic transducers 3, 4 can preferably be located relative to the intervertebral disc 1 so that they transmit ultrasonic fields 3a and 4a which together define a focal area 5 with a substantially planar extension and which are situated substantially in parallel with and in a plane P wherein the intervertebral disc 1 is located.

The ultrasonic transducers 3, 4 can be arranged to transmit ultrasonic fields 3a, 4a with a focal area 5 the extension of which can be varied for adaptation to the size of the intervertebral disc 1 and/or nucleus pulposus 1a.

A diagnostic device 13 may include at least one ultrasonic transducer 14 which is provided, prior to the ultrasound treatment, to transmit an ultrasonic field 14a for registrering the location of the intervertebral disc 1. The position of the ultrasonic transducers 3, 4 relative to the ultrasonic transducer 14 are also known and in this way, their positions relative to the intervertebral disc 1 can be determined. The ultrasonic transducers 3, 4 can be arranged to be controlled depending on information registered in the diagnostic device 13 regarding the current position of the intervertebral disc 1, preferably nucleus pulposus 1a, so that the focal area 5 is moved to coincide with the intervertebral disc 1, preferably nucleus pulposus 1a. The positions of the ultrasonic transducers 3, 4 can e.g. be controlled by changing their positions relative to their attachments. The control can be determined by a computer.

Said control of the ultrasonic transducers 3, 4 can be carried through by means of a control device 15 either automatically or by a surgeon marking on a screen (not shown) a point/an area in nucleus pulposus 1a in which the focal area 5 is desired. A computer (not shown) can determine the necessary parameters in the ultrasonic transducers 3, 4 such that the focal area 5 becomes correct.

A reading device 16 can be provided for registering displacements of the intervertebral disc 1 relative to the ultrasonic transducers 3 and 4 which occur when the

patient moves during treatment. A setting device 17 can be provided to automatically control the ultrasonic transducers 3, 4 to set so that the focal area 5 again will lie in the intervertebral disc 1, preferably nucleus pulposus 1a, after said displacement.

There might also be a non-invasive temperature-supervising device 18 for supervising the temperature in the intervertebral disc 1 during treatment. This temperature-supervising device 18 may cooperate with a control unit 19 which is provided to control the ultrasonic transducers 3, 4 such that undesired temperature changes in the intervertebral disc 1 are prevented during treatment.

The temperature-supervising device 18 may cooperate with the ultrasonic transducer 14 of the diagnostic device 13 for supervising or monitoring the temperature in the intervertebral disc 1 by means of ultrasound.

The ultrasonic transducers 3, 4 are preferably arranged obliquely behind the spine on opposite sides of the spinal cord 6, so that they can transmit their ultrasonic fields 3a, 4a in a direction beside said spinal cord 6 on opposite sides thereof and so that they meet in front thereof in order to together define the focal area 5 in the intervertebral disc 1, preferably nucleus pulposus 1a.

During treatment, a treatment table 20 can be used, which has a support surface 21 for the patient 22. This support surface 21 can be curved or settable into a curved shape such that the space M between the vertebrae 9, 10 at the intervertebral disc 1 to be treated, increases when the patient 22 rests with his or her back against said support surface 21.

The ultrasonic transducers 3, 4 and 14 can be mounted on a frame 23, whereby the mutual positions of said transducers 3, 4 and 14 can be known. Said frame 23 with the transducers 3, 4 and 14 is preferably displaceable relative to the treatment table 20 and the patient 22 for setting the transducers 3, 4 and 14 relative to an intervertebral disc 1, preferably nucleus pulposus 1a, to be treated, in a patient 22 on the treatment table 20.

To avoid disturbances of the ultrasonic fields 3a, 4a transmitted by said transducers 3, 4 and 14, a gasvoid liquid in a liquid container 24 can be located between the transducers and the adjacent skin of the patient 22.

Air between the transducers 3, 4 and 14, the liquid container 24 and adjacent skin can for the same purpose be removed by locating a gel 25 schematically illustrated with broken lines.

Treatment by means of the device described above is shown in the flow chart of fig. 4, whereby the diagnosis is already made, i.e. it is already determined which intervertebral disc 1 should be treated.

By means of the "ultrasound picture" obtained from the diagnostic device 13, the frame 23 and the patient 22 and eventually the ultrasonic transducers 3, 4 are oriented separately so that the angle of incidence of the therapeutic transducers 3, 4 is correct. Hereby, it is achieved that the ultrasonic fields 3a, 4a of the ultrasonic transducers 3, 4 lie in the same plane P as the intervertebral disc 1 to be treated, and so that the therapeutic transducers 3, 4 are directed towards the patient 22 from behind. On the abovementioned screen, a point in the nucleus pulposus 1a is marked in which the focal area 5 (a so called movable focus which is displaced by means of the abovementioned means 12) for the therapeutic transducers 3, 4 shall be located. A computer then establish the requirements for the various transducer elements in the therapeutic transducers 3, 4. Eventually, adjacent bones can be marked as zones which the ultrasonic fields 3a, 4a are not allowed to reach.

Said computer may e.g. deactivate the transducer elements which are closest and reduces thereby the size of the ultrasonic field 3a or 4a in question. This reduction of the ultrasonic field 3a and/or 4a can be compensated with a longer treatment time and/or treatment effect. The "fixed focus" mentioned in the flow chart is the focal area obtained by means of the abovementioned means 11.

It should also be mentioned that instead of ultrasonic transducers, other therapeutic and/or diagnostic transducers, transmitters or applicators, e.g. transducers or transmitters of electromagnetic radiation, can be used in the device described above.

Drugs can be used in connection with and/or after treatment with the abovementioned device, namely pressure reducing/volume decreasing drugs, e.g. steroids or corticon™, and/or dehydrating drugs, e.g. impugan™, and/or antiinflammatory drugs, e.g. voltaren™.

By means of the pressure reducing/volume decreasing drugs, it is possible, in connection with and/or after treatment with ultrasound, to improve the pressure reduction/volume decrease in nucleus pulposus obtained thereby.

By means of the dehydrating drugs, it is possible to improve the removal of fluid from the treatment area in connection with and/or after treatment with ultrasound.

By means of said antiinflammatory drugs, it is possible to oppose inflammations in the treatment area in connection with and/or after treatment with ultrasound.

The invention is not limited to the device described above and illustrated in the drawings, but may vary within the scope of the following claims. Thus, the device may include more than one treatment transducer 2, there may be one, two or another suitable number of ultrasonic transducers and the diagnostic device 13 can operate with something else than ultrasound.

Instead of the patient 22 lying on his back on a treatment table 20, whereby the treatment equipment is situated beneath his or her back, the patient 22 and treatment equipment can be positioned otherwise. Thus, the patient 22 can e.g. be lying on his or her face and the treatment equipment be mounted on an arm permitting location thereof in a treatment position.

REFERENCES

Billard BE, Hynynen K and Roemer R B, 1990, *Effects of physical parameters on high temperature ultrasound hyperhtermia*. Ultrasound in Med. & Biol., 16 (4), 409-420

Buchelt M, Kutschera H-P, Katterschafka T, Kiss H, Schneider B and Ullrich R, 1992, *Erb.YAG and Hol.YAG Laser Ablation of Meniscus and Intervertebral discs*. Lasers in Surgery and Medicine, 12, 375-381

Bush N L, Rivens I, ter Haar G R and Bamber J C, 1993, *Acoustic properties of lesions generated with an ultrasound therapy system*. Ultrasound in Med & Biol, 19 (9), 789-801

Diederich C J and Hynynen K, 1991, *The feasibility of using electrically focused ultrasound arrays to induce deep hyperthermia via body cavities*. IEEE transactions on ultrasonics, ferroelectrics, and frequency control, 38 (3), 207-219

Ebbini E S and Cain C A, 1991, *A Spherical-Section Ultrasound Phased Array Applicator for Deep Localized Hyperthermia*. IEEE Transactions on Biomedical Engineering, 38 (7), 634-643

Ebbini E S, Umemura S-I, Ibbini M and Cain C A, 1988, *A cylindrical-section ultrasound phased-array applicator for hyperthermia cancer therapy*. IEEE transactions on ultrasonics, ferroelectrics, and frequency control, 35 (5), 561-572

Holmer N-G and Lindström K, 198?, Från A-mode till Phased array i *Diagnostiskt ultraljud—Grunderna*, editerad av Holmer, s 65-67

Lele P P, 1980, *Induction of deep, local hyperthermia by ultrasound and electromagnetic fields. - Problems & choices*. Radiation and Environmental Biophysics, 17, 205-217

Linke C A, Carstensen E L, Frizzell L A, Elbadawi A and Fridd C W, 1973, *Localized tissue destruction by high-intensity focused ultrasound*. Arch Surg, 107 (6), 887-891

Sibille A, Prat F, Chapelon J-Y, El Fadil F A, Henry L, Theillère Y, Ponchon T and Cathignol D, 1993, *Extracorporeal ablation of liver tissues by high intensity focused ultrasound*. Oncology, 50, 375-379

Troussier B, Lebas J F, Chirossel J P, Peoc'h M, Grand S, Leviel J L and Phelip X, 1995, *Percutaneous Intradiscal Radio-Frequency Thermocoagulation - A Cadaveric Study*. Spine, 20 (15), 1713-1718

Claims

1. Device for non-invasive treatment of biological tissue, whereby the treatment aim at changing or degenerating said tissue,
characterized in

that a treatment transducer (2) comprises at least one ultrasonic transducer (3 and/or 4) which is provided to treat intervertebral discs (1), preferably nucleus pulposus (1a), by means of ultrasound,
whereby the ultrasonic field of the ultrasonic transducer (3 and/or 4) is focused in said intervertebral disc (1), preferably in nucleus pulposus (1a), for heating the tissue therein to such temperatures that the tissue in the focal area (5) degenerates, whereby the pressure in the intervertebral disc (1) and thus, the pressure against the spinal cord (6), is reduced.

2. Device according to claim 1, **characterized in** that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) is provided to transmit an ultrasonic field (3a and/or 4a) which does not heat biological tissue outside the focal area (5) such that it degenerates.

3. Device according to claim 1 or 2, **characterized in** that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) is provided to transmit ultrasonic waves having a frequency of 0,5 - 2,5 MHz.

4. Device according to any preceding claim, **characterized in** that the ultrasonic transducers (3 and/or 4) of the treatment transducer (2) is provided to transmit an ultrasonic field (3a and/or 4a) which in the focal area (5) heats the tissue to a temperature of 45-80°C.

5. Device according to any preceding claim, **characterized in** that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) is provided to transmit an ultrasonic field (3a and/or 4a) which in the focal area (5) heats the tissue for a time period of 5-60 minutes per treatment.

6. Device according to any preceding claim, **characterized in** that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) is provided to transmit an ultrasonic field (3a and/or 4a), the focal area (5) of which has an extension which is adaptable relative to the space (M) between end plates (7, 8) of the vertebrae (9, 10) surrounding the intervertebral disc (1) such that said focal area (5) can lie between said end plates (7, 8) without heating thereof to tissue-degenerating temperatures.

7. Device according to claim 6, **characterized in**

that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) has means (11) for transmitting an ultrasonic field (3a and/or 4a) the focal area (5) of which has an extension

which is adaptable to said space (M) between the end plates (7, 8), and

that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) further includes means (12) for displacing the focal area (5), adapted preferably as mentioned to the space (M) between the end plates (7, 8), to the intervertebral disc (1), preferably nucleus pulposus (1a).

8. Device according to claim 7, **characterized in**

that said means (11) in the treatment transducer (2) for transmitting an ultrasonic field (3a and/or 4a) with a focal area (5) which is adaptable to the space (M) between the end plates (7, 8), includes transducer elements having concave spherical transducer surfaces, and
that said means (12) in the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) for displacing the focal area (5), includes transducer elements of the phased array type.

9. Device according to any preceding claim, **characterized in** that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) have a plurality of means (12), preferably transducers of the phased array type, of which one or more can be deactivated or put out of operation for reducing the extension of the ultrasonic field (3a and/or 4a) if required for preventing said ultrasonic field from heating biological tissues outside the intervertebral disc (1) to tissue-degenerating temperatures.

10. Device according to any preceding claim, **characterized in** that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) is located to transmit an ultrasonic field (3a and/or 4a) with a focal area (5) with a substantially planar extension and which is situated substantially in parallel with and in a plane (P) wherein the intervertebral disc (1) is located.

11. Device according to any preceding claim, **characterized in** that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) is arranged to transmit an ultrasonic field (3a and/or 4a) with a focal area (5) the extension of which is variable for adaptation to the size of the intervertebral disc (1) and/or nucleus pulposus (1a).

12. Device according to any preceding claim, **characterized in**

that a non-invasive temperature-supervising device (18) is provided, preferably by means of ultrasound, to supervise the temperature in the intervertebral disc (1) during treatment, and
that a control unit is provided to control the ultrasonic transducers (3 and/or 4) of the treatment transducer (2) such that undesired temperature changes in the intervertebral disc (1) are prevented.

13. Device according to any preceding claim, **characterized in**

that a diagnostic device (13) is provided for registering the location of the intervertebral disc (1), preferably nucleus pulposus (1a), relative to the ultrasonic transducer (3 and/or 4) of the treatment transducer (2), and
that the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) is arranged to be controlled depending on information registered in the diagnostic device (13) so that the focal area (5) of its ultrasonic field (3a and/or 4a) is moved to coincide with the intervertebral disc (1), preferably nucleus pulposus (1a).

14. Device according to claim 13, **characterized in** that the diagnostic device (13) includes an ultrasonic transducer (14) which transmits an ultrasonic field for registering the location of the intervertebral disc (1), preferably nucleus pulposus (1a), relative to the treatment transducer (2).

15. Device according to any preceding claim, **characterized in**

that a reading device (16) is provided for registering displacements of the intervertebral disc (1) relative to the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) which occur when the patient moves during treatment, and
that a setting device (17) is provided to control the ultrasonic transducer (3 and/or 4) of the treatment transducer (2) to set so that the focal area (5) of the ultrasonic field (3a and/or 4a) will lie in the intervertebral disc (1), preferably nucleus pulposus (1a), after displacement thereof.

16. Device according to any preceding claim, **characterized in** that the treatment transducer (2) comprises at least two ultrasonic transducers (3, 4) which each transmit an ultrasonic field (3a and 4a respectively) which together define the focal area (5) wherein the tissue is heated to temperatures at which it degenerates, and which each separately does not have such high effect that they degenerate tissue outside the intervertebral disc (1).

17. Device according to claim 16, **characterized in** that the ultrasonic transducers (3, 4) forming part of the

treatment transducer (2) are located during treatment obliquely behind the spine on opposite sides of the spinal cord (6), so that they can transmit their ultrasonic fields (3a, 4a) in a forward direction past said spinal cord (6) on opposite sides thereof and so that they meet in front thereof in order to together define the focal area (5) in the intervertebral disc (1), preferably nucleus pulposus (1a).

18. Device according to any preceding claim, **characterized in** that a treatment table (20) for use during treatment of intervertebral discs (1), preferably nucleus pulposus (1a), has a support surface (21) which is curved or settable into a curved shape such that the space between the vertebrae (9, 10) at the intervertebral disc (1) to be treated, increases when the patient (22) is supported by said support surface (21).

19. Device according to any preceding claim, **characterized in**

that the ultrasonic transducers (3, 4) of the treatment transducer (2) and a diagnostic device (13) having an ultrasonic transducer (14) are mounted on a frame (23) relative to a treatment table (20), whereby the mutual positions between said transducers (3, 4 and 14) are known, and
that the frame (23) is displaceable relative to a patient (22) for setting said transducers (3, 4 and 14) relative to an intervertebral disc (1), preferably nucleus pulposus (1a), of the patient (22).

20. Device according to any preceding claim, **characterized in** that the ultrasonic transducers (3, 4) of the treatment transducer (2) are separately controllable relative to their attachments.

21. Device according to any preceding claim, **characterized in** that between the ultrasonic transducers (3, 4) of the treatment transducer (2) and an ultrasonic transducer (14) in a diagnostic device (13) as well as adjacent skin of a patient (22) to be treated, there is provided a gasvoid liquid in a liquid container (24).

22. Device according to claim 21, **characterized in** that a gel (25) is provided for removing air between said transducers (3, 4 and 14) and the liquid container (24) as well as at adjacent skin.

23. Device according to any preceding claim, **characterized in** that other therapeutic and/or diagnostic transducers, transmitters or applicators, e.g. transducers or transmitters of electromagnetic radiation, are used in the device instead of the ultrasonic transducers.

24. Use of pressure reducing/volume decreasing drugs, e.g. steroids or cortison™, and/or dehydrating drugs, e.g. impugan™, and/or antiinflammatory drugs, e.g. voltaren™, in connection with and/or after treatment of intervertebral discs with ultrasound.

25. Use according to claim 24 of said drug or drugs in connection with the treatment with ultrasound by focusing an ultrasonic field in an intervertebral disc (1), preferably in nucleus pulposus (1a), for heating the tissue therein to such temperatures that the tissue in the focal area (5) degenerates, whereby the pressure in the intervertebral disc (1) and thus, the pressure against the spinal cord (6), is reduced.

26. Use of pressure reducing/volume decreasing drugs, e.g. steroids or cortison™, and/or dehydrating drugs, e.g. impugan™, and/or antiinflammatory drugs, e.g. voltaren™, in connection with and/or after treatment of intervertebral discs with ultrasound by means of the device according to any of claims 1-22.

Fig. 1

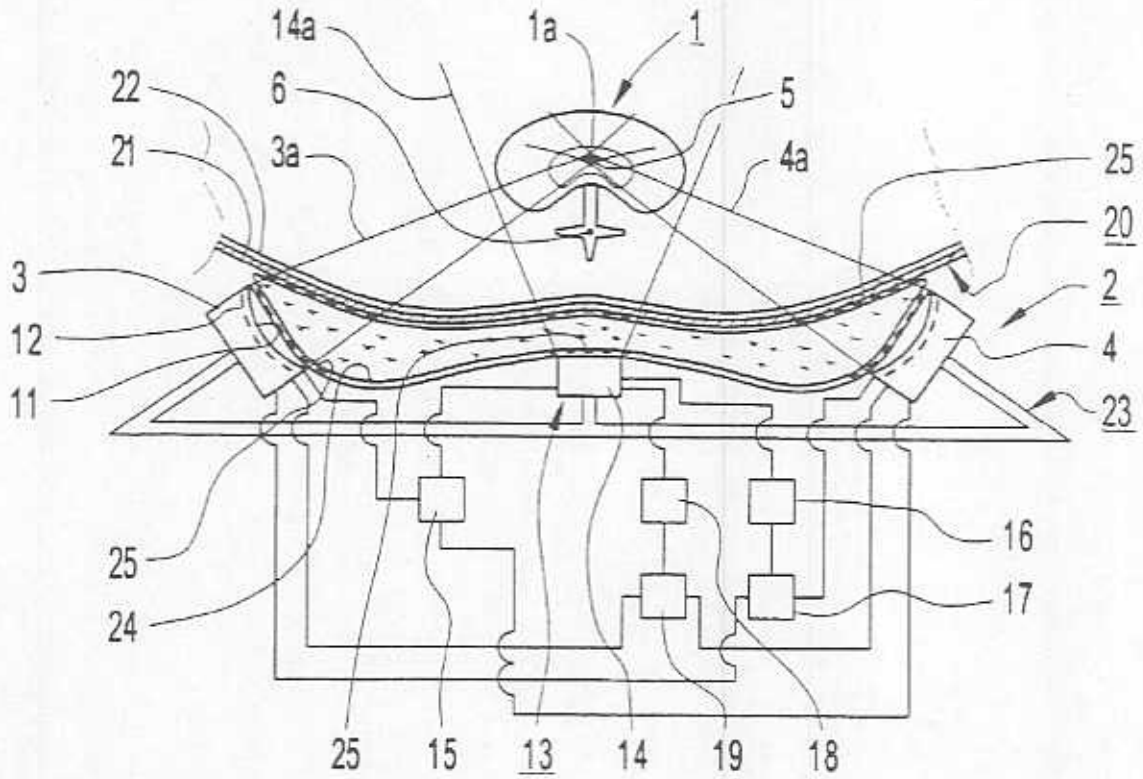

14a
1a
1
22
6
5
21
3a
4a
25
20
3
2
12
4
11
23
16
25
17
24
25
15
13
14
19
18

Fig. 3

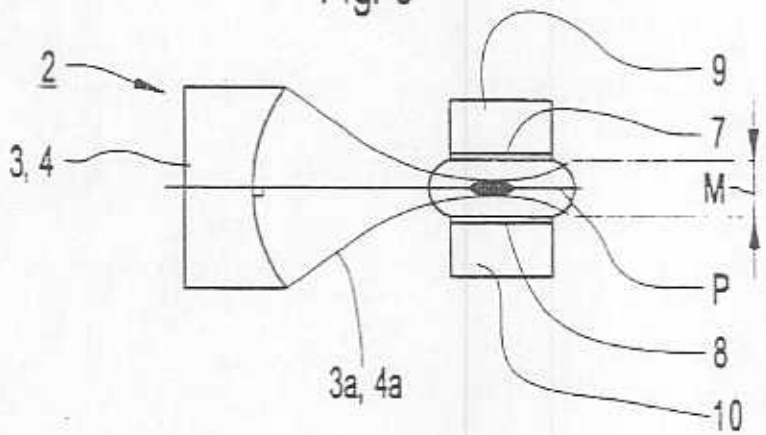

2
9
7
3, 4
M
P
8
3a, 4a
10

Fig. 2

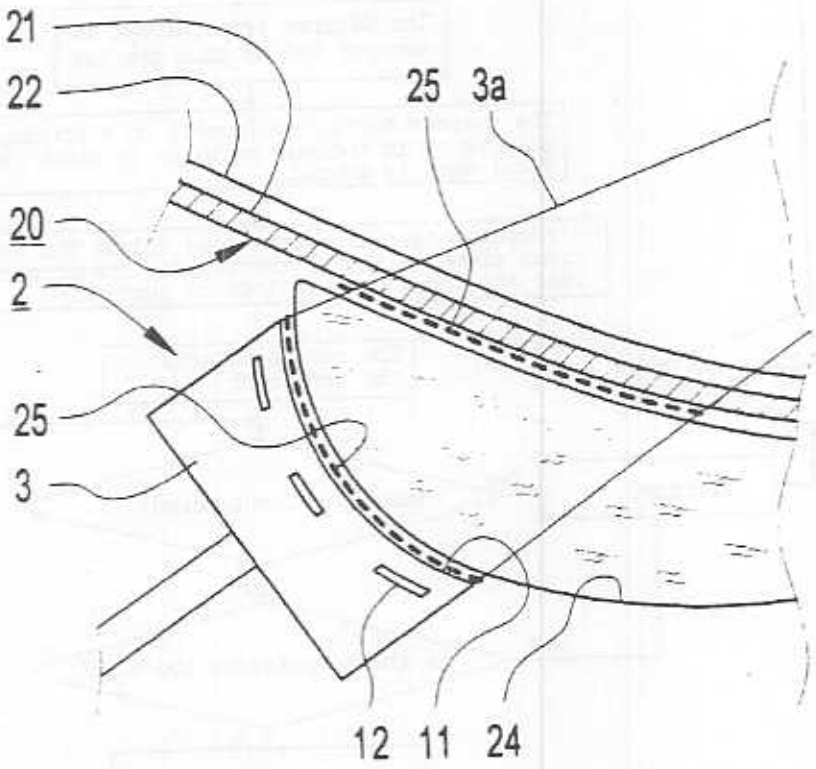


Fig. 4

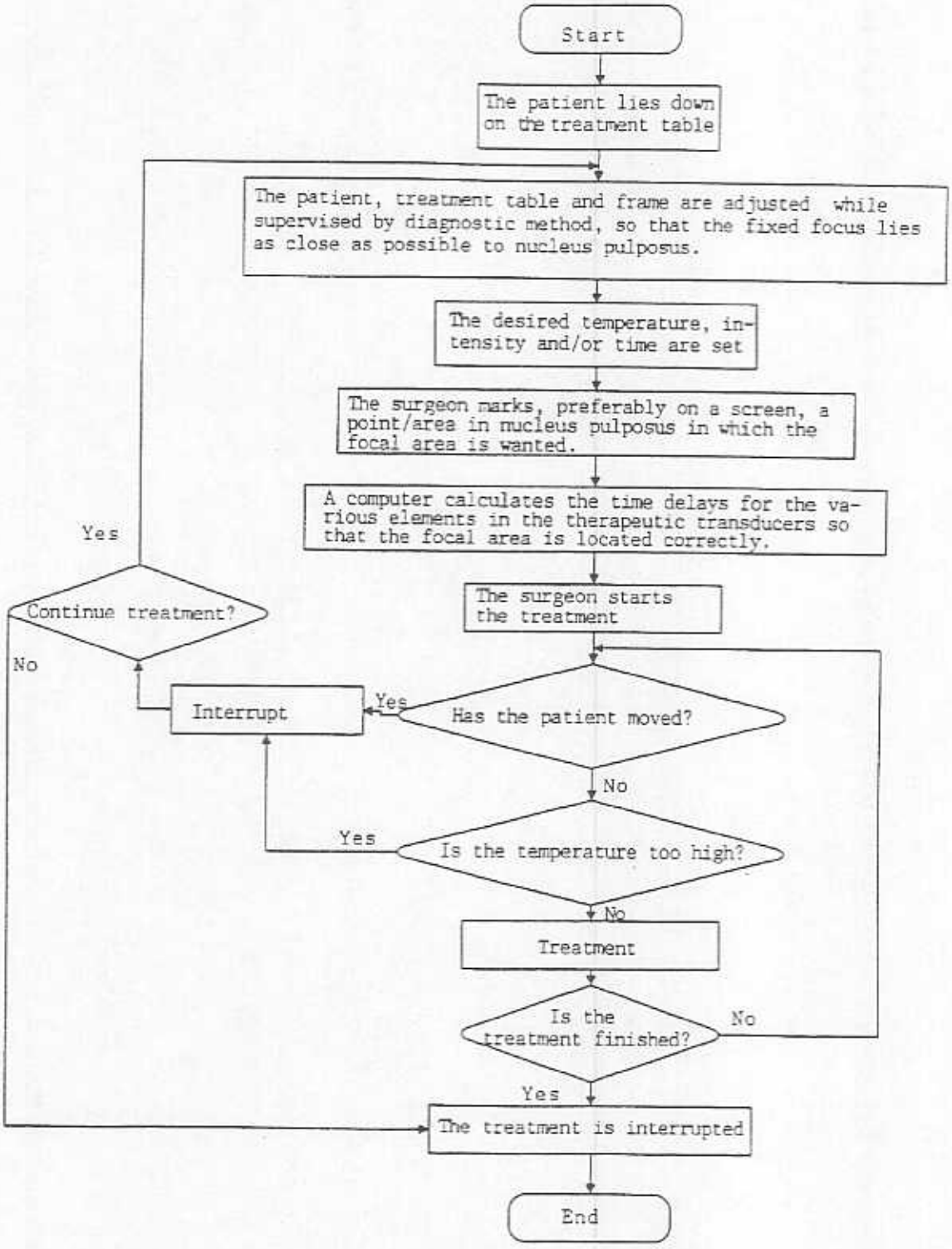
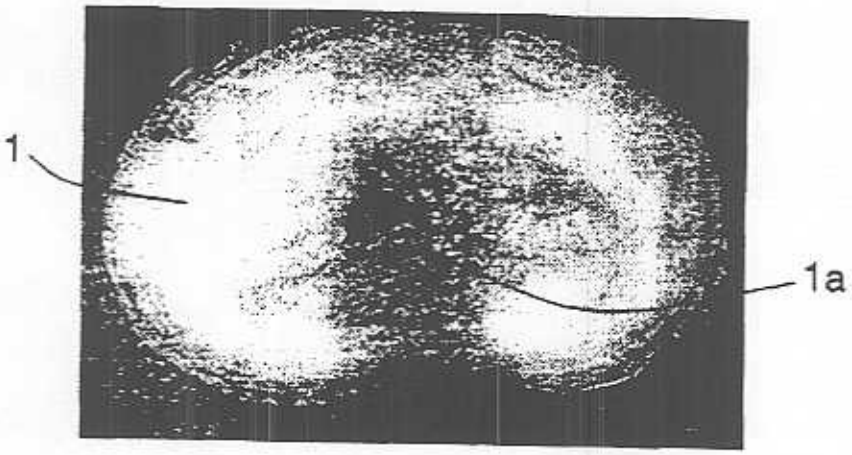

Start
The patient lies down on the treatment table
The patient, treatment table and frame are adjusted while supervised by diagnostic method, so that the fixed focus lies as close as possible to nucleus pulposus.
The desired temperature, intensity and/or time are set
The surgeon marks, preferably on a screen, a point/area in nucleus pulposus in which the focal area is wanted.
A computer calculates the time delays for the various elements in the therapeutic transducers so that the focal area is located correctly.
The surgeon starts the treatment
Has the patient moved?
Yes
Interrupt
No
Is the temperature too high?
Yes
No
Treatment
Is the treatment finished?
No
Yes
Continue treatment?
Yes
No
The treatment is interrupted
End

Fig. 5



(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 872 262 A3

(12) EUROPEAN PATENT APPLICATION

(88) Date of publication A3:
10.11.1999 Bulletin 1999/45

(43) Date of publication A2:
21.10.1998 Bulletin 1998/43

(51) Int. Cl.[6]: **A61N 7/02**

(21) Application number: **98106818.2**

(22) Date of filing: **15.04.1998**

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: **18.04.1997 SE 9701449**

(71) Applicant:
Scandimed International AB
275 37 Sjöbo (SE)

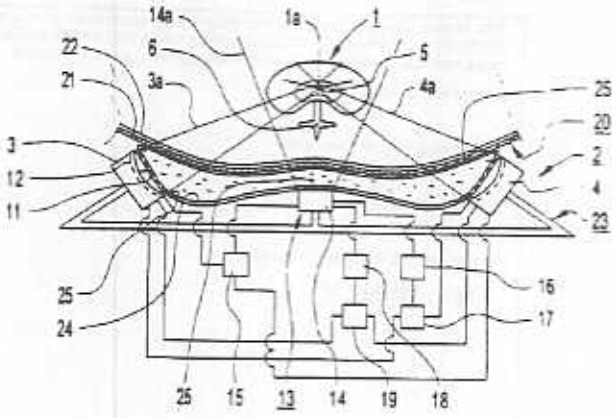
(72) Inventors:
- **Lidgren, Lars**
  227 31 Lund (SE)
- **Strömqvist, Björn**
  237 31 Bjärred (SE)
- **Severson, Johan**
  224 58 Lund (SE)

(74) Representative:
Wagner, Karl Heinz
H. Wagner & Co. AB
Norra Vallgatan 72
211 22 Malmö (SE)

(54) Device for non-invasive treatment of biological tissue

(57) The present invention relates to a device for non-invasive treatment of biological tissue, whereby the treatment aim at changing or degenerating said tissue. This device has a treatment transducer (2) comprising at least one ultrasonic transducer (3 and/or 4) which is provided to treat intervertebral discs (1), preferably nucleus pulposus (1a), by means of ultrasound, whereby the ultrasonic field of the ultrasonic transducer (3 and/or 4) is focused in said intervertebral disc (1), preferably in nucleus pulposus (1a), for heating the tissue therein, to such temperatures that the tissue in the focal area (5) degenerates, whereby the pressure in the intervertebral disc (1) and thus, the pressure against the spinal cord (6) is reduced.

Fig. 1



EP 0 872 262 A3

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number EP 98 10 6818

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Y	WO 93 17646 A (SIEMENS AG) 16 September 1993 (1993-09-16)	1-5,7-9, 11-16, 20,21	A61N7/02
A	* page 8, line 26 - line 29; figure 1 * * page 10, line 18 - line 29; figure 2 * * page 19, line 13 - line 20; figure 4 * * page 25, line 1 - line 4 * ---	6,10,19	
Y	US 5 571 147 A (SLUIJTER MENNO E ET AL) 5 November 1996 (1996-11-05) * column 2, line 44 - line 51; figure 1 * ---	1-5,7-9, 11-16, 20,21	
D,A	US 5 501 655 A (ROLT KENNETH D ET AL) 26 March 1996 (1996-03-26) * column 3, line 65 - column 4, line 14; figure 1 * * column 12, line 15 - line 21 * ---	1-3,5-9, 11,16,17	
A	US 4 513 749 A (HUSSON DIDIER ET AL) 30 April 1985 (1985-04-30) * column 4, line 19 - line 39; figure 3 * --- -/--	12	

TECHNICAL FIELDS SEARCHED (Int.Cl.6)

A61N
A61G
A61B

INCOMPLETE SEARCH

The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.

Claims searched completely :

Claims searched incompletely :

Claims not searched :

Reason for the limitation of the search:

see sheet C

Place of search	Date of completion of the search	Examiner
THE HAGUE	8 September 1999	Mayer, E

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C07)

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 98 10 6818

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A	US 5 418 990 A (RISASEN BORGE) 30 May 1995 (1995-05-30) * column 5, line 32 - line 39; figures 1,4,7 *	18	
A	US 4 813 402 A (REICHENBERGER HELMUT ET AL) 21 March 1989 (1989-03-21) * column 5, line 27 - line 54; figure 1 *	21,22	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)

EPO FORM 1503 03.82 (P04C10)

European Patent Office

INCOMPLETE SEARCH
SHEET C

Application Number
EP 98 10 6818

Claim(s) searched completely:
1-22

Claim(s) not searched:
24-26

Reason for the limitation of the search (non-patentable invention(s)):

Article 52 (4) EPC - Method for treatment of the human or animal body by surgery

---

Further limitation of the search

Claim(s) searched incompletely:
23

Reason for the limitation of the search:

With the word "applicator", claim 23 relates to an undefined type of medical apparatus, which appears to include an extremely large number of possible devices, e.g. any type of medical device merely comprising 1 applicator. Therefore the claim contains so many options that a lack of clarity (and conciseness) within the meaning of Article 84 EPC arises to such an extent as to render a meaningful search of the claim impossible.

It is to be submitted that by disclaiming the electroacoustic transducers as specified in claim 1, claim 23 is actually an independent claim.

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 98 10 6818

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

08-09-1999

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9317646 A	16-09-1993	DE 4207463 A	23-09-1993
		DE 59306276 D	28-05-1997
		EP 0630220 A	28-12-1994
		JP 7504339 T	18-05-1995
		US 5624382 A	29-04-1997
		US 5759162 A	02-06-1998
US 5571147 A	05-11-1996	US 5433739 A	18-07-1995
US 5501655 A	26-03-1996	WO 9319705 A	14-10-1993
US 4513749 A	30-04-1985	EP 0125309 A	21-11-1984
		JP 60500122 T	31-01-1985
		WO 8401890 A	24-05-1984
US 5418990 A	30-05-1995	WO 9215272 A	17-09-1992
US 4813402 A	21-03-1989	DE 3605277 A	20-08-1987
		EP 0234366 A	02-09-1987
		JP 2091727 C	18-09-1996
		JP 8004596 B	24-01-1996
		JP 62192150 A	22-08-1987
		US 4962752 A	16-10-1990
		EP 0256202 A	24-02-1988
		JP 63051853 A	04-03-1988

EPO FORM P0459